FETAL DOPPLER STUDY OF UMBILICAL ARTERY, MIDDLE CEREBRAL ARTERY AND UTERINE ARTERY AS PREDICTORS OF ADVERSE PERINATAL OUTCOME IN FETAL GROWTH RESTRICTION

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled "**FETAL DOPPLER STUDY OF UMBILICAL ARTERY, MIDDLE CEREBRAL ARTERY AND UTERINE ARTERY AS PREDICTORS OF ADVERSE PERINATAL OUTCOME IN FETAL GROWTH RESTRICTION**" is a bonafide record work done by **Dr. S. SREERANJANI** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for M.D Branch II – Obstetrics & Gynaecology.

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DECLARATION

I, **Dr. S. SREERANJANI** solemnly declare that the dissertation titled "**FETAL DOPPLER STUDY OF UMBILICAL ARTERY, MIDDLE CEREBRAL ARTERY AND UTERINE ARTERY AS PREDICTORS OF ADVERSE PERINATAL OUTCOME IN FETAL GROWTH RESTRICTION**" has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of M.D degree Branch – II (Obstetrics & Gynecology) to be held in April 2012.

Place : Madurai **Dr. S. SREERANJANI**

Date :

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CONTENTS

ABBREVIATIONS

IUGR	Intra Uterine Growth Restriction
LBW	Low Birth Weight
USG	Ultra Sono Gram
FGR	Fetal Growth Restriction
FL	Femur Length
AC	Abdomen Circumference
HC	Head Circumference
DV	Ductus Venosus
IVC	Inferior Vena Cava
SVC	Superior Vena Cava
PI	Pulsatality Index
RI	Resistance Index
S/D	Systolic Diastolic Ratio
UA	Uterine Artery
EDF	End Diastolic Flow
RDF	Reversal of Diastolic Flow
MCA	Middle Cerebral Artery

ABSTRACT

FETAL DOPPLER STUDY OF UMBILICAL ARTERY,MIDDLE CEREBRAL ARTERY AND UTERINE ARTERY AS PREDICTORS OF ADVERSE PERINATAL OUTCOME IN FETAL GROWTH RESTRICTION

AIM AND OBJECTIVES:

- To study the association between the severity of IUGR and abnormal Doppler velocimetry of the umbilical,middle cerebral and uterine artery
- To evaluate the predictive value of Doppler studies in IUGR with relevance to perinatal outcome.
- To evaluate the efficacy of Doppler in the management of patients with IUGR.

METHODOLOGY:

Prospective observational study of singleton pregnant women irrespective of age or parity complicated by IUGR were enrolled during the study period from OCTOBER 2010 to NOVEMBER 2011.

RESULTS AND ANALYSIS:

Out of the 100 patients studied,77% belonged to age group 20-30 yrs,13% were above 30 yrs and 10% were <20yrs.46% of them were primi and remaining multipara.Among the various etiology studied,34% had h/o gestational hypertension,31% had no specific history,11% had association with anemia,9% had heart disease and remaining had placenta previa or chronic maternal disease. 71% had weight gain between 6-10 kg whereas 9% had weight gain <5kg.24% had severe oligoamnios whereas 41% had reduced liquor.The sensitivity,specificity,positive predictive and negative predictive value of uterine artery in predicting perinatal outcome in IUGR is 68.75%,54.68%,61.1% and 84.37%. The sensitivity,specificity,positive

predictive and negative predictive value of umbilical artery is 70.37%,93.15%,79.16% and 89.47%. The sensitivity,specificity,positive predictive and negative predictive value of middle cerebral artery 63.63%,100%,100% and 90.69%.

CONCLUSION:

Doppler velocimetry can be an important adjunct to conventional antepartum surveillance tests on patients with IUGR foetuses.

INTRODUCTION

Intrauterine growth is an important sign of fetal wellbeing. IUGR complicates 3-5% of pregnancies. It contributes significantly to perinatal morbidity and mortality.

Intra uterine growth restriction is a common clinical sign of chronic fetal hypoxemia. It is difficult to differentiate between suboptimal fetal growth due to intra uterine starvation and adequate growth of a constitutionally small infant.

Antepartum surveillance tests to evaluate fetal health have been the focus of intense interest for more than three decades. There are many tests available today each with its advantages and disadvantages.

Doppler plays an important role in IUGR where hemodynamic rearrangements occur in response to fetal hypoxemia. It is now proved that significant Doppler changes occurs with reduction in fetal grow at a time when the fetal well being tests are still normal.

Early and accurate diagnose of IUGR may reduce the mortality and morbidity of fetuses with this condition. Successful perinatal outcome depends on proper management in the antepartum, intrapartum and neonatal period. The obstetricians must weigh the balance between

1. Conservative management in a potentially hostile environment

versus.

2. Intervention which may lead to neonatal morbidity.

This study explores the predictive value of fetal Doppler study of umbilical, middle cerebral and uterine arteries on diagnosing the adverse perinatal outcome in patients with IUGR.

AIMS AND OBJECTIVES

a) To study the association between the severity of IUGR and abnormal Doppler velocimetry of the umbilical, middle cerebral and uterine artery.
b) To evaluate the predictive value of Doppler studies in IUGR with relevance to perinatal outcome.
c) To evaluate the efficacy of Doppler in the management of patients with IUGR.

REVIEW OF LITERATURE

Extensive clinical and basic investigations have been undertaken during the past 30 years to clarify and resolve the reproductive problems associated with impaired fetal growth. Despite this effort, confusion and imprecision persist regarding the definition, diagnosis and appropriate care of a pregnancy suspected of IUGR. It is appropriate, therefore, to review recent findings in the study of IUGR.

In 1961, WARKANY and EOLO WORKERS reported normal values for infant weights, lengths and head circumference and defined fetal growth restriction.

In 1962, WHO introduced the term ‘low birth weight’ for all babies weighing less than 2500 gms as a single category.

In 1963, LUBCHENCO and co workers from Denwer published detailed comparisons of gestational age to birth weight in an effort to derive norms for expected fetal size and therefore growth at a given gestational week.

BATTALGIA and coworkers in 1967 then classified small for gestational age infants as those, whose weights were below 10^{th} percentile for their gestational age.

USHER & MCLEAN in 1969 proposed that fetal growth, standards should be based on normal limits defined by +2 standard deviations.

In 1969, the term 'preterm' was used to indicate gestational age of less than 37 completed weeks (259 days). However the LBW babies include both preterm and those born at term but weighing less than 2500 gms. Therefore, the term IUGR should more strictly refer to fetuses that all small for gestational age and display other signs of chronic hypoxia or failure to thrive. The assignment of a birth weight percentile requires an accurate assessment of gestational age and adjustment for gender, race and altitude. The current incidence of LBW in Indian population in 28% (Thambiraja 1992). The current incidence of IUGR in Indian population 3-5%.

Christian Andreas Doppler and the Doppler Theory :

The Doppler effect is defined as the observed changes in frequency of transmitted sound waves when relative motion exists between the source of the wave and observer. The frequency increases when source and the observer move closer and decrease when they move apart. This phenomenon bears the name of its discoverer Christian Andreas Doppler, an Australian Mathematician and physicist.

The first pulsed wave Doppler equipment was developed by the Seattle Research team. Donald Baker, Dennis Watkins and John Rein began working on this project in 1966 and produced one of the first pulsed Doppler devices. The Seattle team also pioneered the construction of Duplex instrumentation. Based on mechanical sector scanning head in which a single transducer crystal performs both imaging and Doppler functions on a time- sharing basis, the Duplex Doppler technique allowed the USG operator to determine for the first time the target of Doppler Insonation. This development is of critical importance in Obstetric and Gynecological applications, as such range discrimination allow reliable Doppler interrogation of a deep lying circulation such as that of the fetus and of the maternal pelvic organs.

Development of colour Doppler USG :

Spectral Doppler USG interrogates along the single line of ultrasound beam transmission. The hemodynamic information thus generalized is limited to unidimensional flow velocity characterization from the target area. This limitation provided the impetus to develop a method for depiction of flow in a two dimensional plane in a real time.

The development of real line two dimensional colour Doppler USG therefore represents a major technologic break through, which becomes possible because of introduction of two critical pieces of technology for processing the Doppler ultrasound and signal. First were the Doppler sonographic applications by ANGELSON and KRISTOFFERSON of the sophisticated filtering technique of the moving target indicator used in radar system. This filter allows removal of high amplitude / low velocity clutter signals generated by movement of tissues structure and vessel walls. The second was development of auto correlation technique by Namekawa et al. The autocorrelater is capable of processing mean Doppler phase shift data from two dimensional scan areas in real time.

Introduction of Doppler USG to Obstetrics and Gynaecology :

The first obstetric application of Doppler USG consisted in detection of fetal heart movements. Originally developed for fetal heart rate detection, the technique was further developed for non invasive continuous electronic monitoring of the fetal heart rate. Currently, they contribute the most common uses of Doppler USG in obstetrics. The system is based on utilizing relatively simple continuous wave Doppler USG to determine the fetal heart rate from the fetal cardiac wall or valvular motion.

The first application of Doppler velocimetry in obstetrics was reported by FITZGERALD and DRUMM and MC CALLUM et al. The former are recognized as the first group to publish a peer recovered article in this field. These publications were followed by an era of impressive research productivity during which investigators extended the use of Doppler velocimetry for assessing various component of fetal and maternal circulations. These studies utilized continuous wave and duplex pulsed wave Doppler technology.

Use of two dimensional colour Doppler flow mapping techniques in Obstetrics was reported by Devore and Associates and Maulik and associates. In both studies Doppler flow mapping was used to characterize fetal cardiac flow dynamics. Taylor and Colleagues were the first to characterize the Doppler waves from the ovarian and uterine arterial circulations utilising pulse duplex Dopper instrumentation.

Intra Uterine Growth Restriction :

Human fetal growth is characterized by sequential patterns of tissue and organ growth differentiaton and maturation. Development is determined by maternal provision of substrate, placental transfer of these substrates and fetal growth potential governed by the genome.

Lin and Santolaya – Forgans (1998) have divided cell growth into three consecutive phases. The initial phase of hyperplasia occurs in the first 16 weeks and is characterised by a rapid increases in cell number. The second phase, which extends upto 32 weeks, includes both cellular hyperplasia and hypertrophy. After 32 weeks fetal growth is by cellular hypertrophy and it is during this phase that most fetal fat and glycogen deposition takes place. The corresponding fetal growth rates during these three phases are 5 gm/day at 15 weeks, 15-20g/day at 24 weeks and 30-35gm / day at 34 weeks.

The ability to reach optimal birth weight depends on

a) Fetal growth potential and

b) Fetal environment

Birth weight depends on gestational age and fetal growth weight. Infants of low birth weight may be classified as belonging to one of the following 3 groups

a) Preterm and appropriate for gestational age

b) Preterm and small for gestational age

c) Term and growth retarded

IUGR represents a continuum of various condition that ultimately result in the failure of fetus to attain its inherent growth potential. IUGR is defined as a pathological decrease in fetal growth rate.

The term IUGR designates birth weight lesser than 10^{th} percentile for the gestational age.

IUGR is associated with substantive perinatal morbidity and mortality rates. Fetal demise, birth asphyxia, meconium aspiration and neonatal hypoglycemia and hypothermia are all increased as is the prevalence of abnormal neurological development. Compared with appropriately grown counterparts, perinatal mortality rates in growth restricted neonates are 6-10 times greater ; perinatal morbidity rates as high as 120 / 1000 for all cases of IUGR have been reported.

CLASSIFICATION:

Campbell and Thomas described the use of the sonographically determined head to abdomen circumference ratio to differentiate growth restricted fetuses type I or symmetric FGR corresponds to fetuses that are symmetrically small and have normal HC / AC and FL /AC. Type II or asymmetrical FGR corresponds to fetuses that have an AC that is smaller than the HC and FL resulting in abnormality high HC / FC and FL / AC ratios. Type III or intermediate FGR corresponds to fetuses that are initially symmetric but become asymmetrical later on pregnancy. The main problem with this classification is that the three groups include normal and pathologically restricted FGR and therefore prognostic value is poor.

Symmetric IUGR	Asymmetric IUGR
1. Symmetrically small	Head larger than abdomen
2. Ponderal index – Normal	Low
3. HC : AC and FL : AC ratio Normal	Elevated
4. Etiology : Genetic disease or infection – Intrinsic to fetus	Chronic placental insufficiency – Extrinsic to fetus
5. Total cell number – less Cell size – Normal	Normal Smaller
6. Neonatal course – complicated with poor prognosis	Usually uncomplicated having good prognosis.

Another method to classify FGR fetuses is based on the origin of the problem and subdivides them into four categories- “ Intrinsic, Extrinsic, combined and idiopathic”. “Intrinsic” FGR occurs when the fetuses are small due to fetal condition such as viral infections or chromosomal abnormalities “Extrinsic” FGR occurs when the growth failure is due to an element outside of the fetus such as a placental condition or a maternal disease. “Combined” FGR occurs when there are extrinsic and intrinsic factors causing the growth failure and “Idiopathic” FGR when the cause of the fetal growth failure is unknown.

Etiology : The causes of FGR can be divided into four groups.

1. Maternal 2. Fetal 3. Placental 4. Unknown

Maternal :

a) Constitutional : Small women, maternal genetic and racial background.

b) Maternal nutrition before and during pregnancy, critical substrate requirement for fetal growth such as glucose, amino acids and oxygen are deficient during pregnancy.

c) Maternal disease – Anemia, hypertension, thrombophilia heart disease, chronic renal disease, collagen vascular disease.

d) Toxins – alcohol, smoking, cocaine, heroin, drugs

Fetal :

a. Structural anomalies either cardiovascular, renal or others

b. Chromosomal abnormality – triploidy, aneuploidy, Trisomy, (13,18,21), Turner's syndrome

c. Infection – Torch, malaria, CMV

d. Multiple pregnancy

Placental

a) Placenta previa

b) Abruptio placenta

c) Circumvallete placenta

d) Infarction

Unknown :

Cause is unknown in about 40% cases.

Normal growth and development of uteroplacental circulation during pregnancy

During the first 12 weeks of pregnancy, cytotrophoblast invade the spiral arterial walls in the decidua and replace the endothelium and muscular media with a matrix of cytoprophoblast and fibrinoid and fibrous tissue. The fibrinoid material is a complex of maternal fibrin and other plasma constituents plus proteinaceous material derived from the trophoblastic cells. Beginning at about 12 weeks of gestation and continuing through out the remainder of the second trimester, the endovascular trophoblast move in to the myometrial segments of spiral arteries. Once again the trophoblast replace the endothelium and establish themselves in the muscular media. The elastic and muscular tissue of the myometrial segments of the spiral arteries is gradually lost and replaced with fibrinoid material. The condition, along with increase in blood flow and the associated haemodynamic forces, convert the entire length of the spiral arteries from small muscular arteries to dilated, tortuous uteroplacental vessels. At term these changes can be seen at the distal portion of the radial arteries. In all approximately, 100 – 150 converted spiral arteries supply the placental bed. There is increase in flow from 100 ml / min to 800 ml / min.

Abnormal development of uteroplacental circulation in the presence of IUGR.

According to Brosen et al, Robertson et al and Khong et al a lack of endovascular infiltration by trophoblast into the myometrial portion of the placental bed spiral arteries a consistent finding in the presence of IUGR. Classically it is held that second wave of endovascular trophoblastic invasion that proceeds in myometrial segments of the spiral arteries from about 15 weeks, does not occur in patients who will develop fetal growth restriction. Lack of physiological conversion is not only apparent in the myometrial segments of spiral arteries but also in the decidual parts of some of the vessels, so that a proportion of spiral arteries completely fail to undergo trophoblastic invasion and physiological changes. Since unconverted vessels retain ‘high resistance/ low capacitance’ properties, the effect on maternal blood supply to the placenta may be dramatically low. These may manifest as impaired growth of the baby.

The persistance of high resistance to flow after 24-26 weeks of gestation provides the rationale to investigate the placental circulation by Doppler and to predict development of fetal growth restriction.

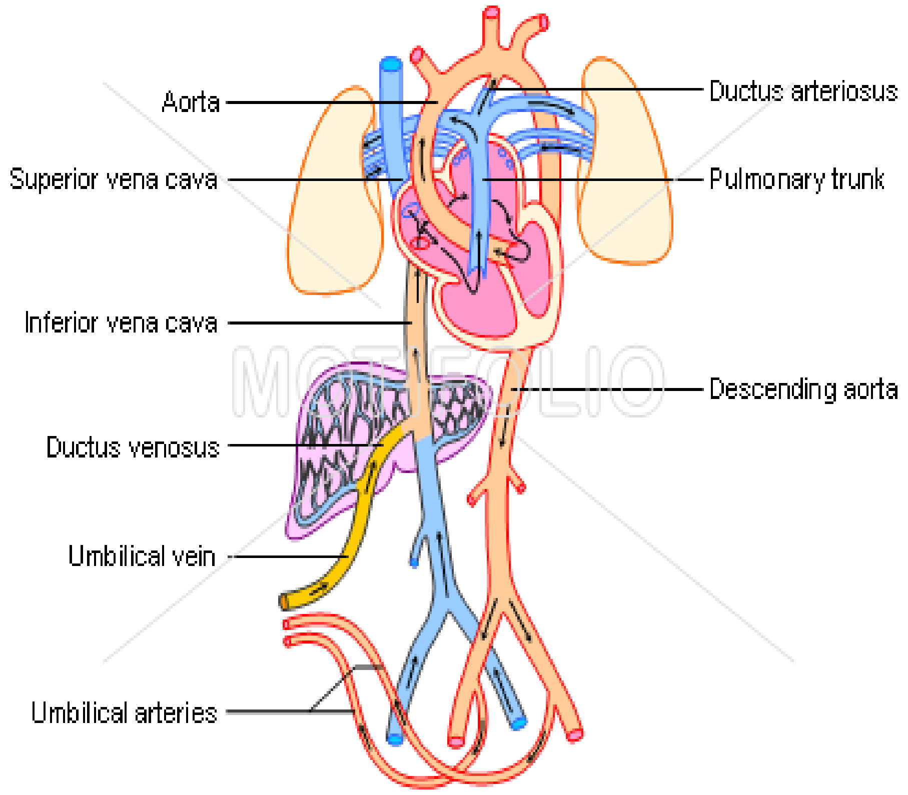
Pathophysiology :

Interference with the placental nutrient supply can affect all aspects of placental function. Mild placental disease is more likely to affect organ function and maturation at the cellular level, with little perceivable growth delay perinatally, but may affect adult health by fetal programming. With more severe placental disease, fetal growth delay and adaptive organ responses become evident in utero. Exhaustion of the placental and fetal adaptive potential leads to decompensation, with variable progression and manifestations on the fetal organ systems.

Mechanism of placental dysfunction :

Early interference with placentation affects all level of placental and fetal development and culminates in the most severe clinical picture. Typically the trophoblastic invasion is confined to the decidual portion of the myometrium and the spiral and radial arteries do not transform into low resistance vessels. Altered

Fetal circulation



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expression of vaso active substance increase vascular reactivity, and if hypoxia- simulated angiogenesis is inadequate placental autoregulation becomes deficient.

Maternal placental floor infarcts and fetal villous obliteration and fibrosis increase placental blood flow substance, producing a maternal – fetal placental perfusion mismatch that decrease the effective exchange area. With progressive vascular occlusion fetoplacental flow resistance is increased throughout the vascular bed which is the metabolically active placental mass and nutrient exchange decreases or in outgrown.

The severity of placental vascular dysfunction is clinically assessed in the fetal and maternal compartments with Doppler ultrasound. Abnormal umbilical flow patterns indicate an increased rate of hypoxemia and acidemia proportional to the severity of Doppler abnormality.

Fetal response in Major organ systems :

Vascular and metabolic disturbances within the placenta lead to alterations in many fetal organ systems. Changes in fetal blood flow are related to placental resistance, fetal oxygenation, organ autoregulation and vascular reactivity.

In the compensated hypoxemic state, fetal cardiac output is increased and organ autoregulation maintained. The response of the fetal trunk and cerebral circulation to hypoxemia differ from each other. The peripheral arteries constrict and truncal resistance increases as evident by the elevated umbilical, thoracic and descending aorta Doppler resistance indices ("hind limb reflex") that account for most of the increase in right ventricular after load. The fetal cerebral circulation dilates in response to hypoxemia. Fetal cerebral vasodilatation is reflected in decreased Doppler indices (brain sparing) and reduces left ventricular after load.

Enhanced blood flow to individual organs is documented in the myocardium, adrenal glands, spleen and liver. Conversely, blood flow resistance in the peripheral pulmonary arteries, celiac axis, mesenteric vessels, kidneys and femoral and iliac vessels increases. The overall effect is an improved distribution of well oxygenated blood to vital organs, with preferential streaming of descending aorta blood flow to the placenta for reoxygenation. In contrast, blood flow to the organs that are not vital for fetal survival is decreased.

Further, increased circulating levels of endothelin, arginine, vasopressin, norepinephrine, epinephrine, vasoactive intestinal peptide, and atrial natriuretic peptide are related directly to the severity of the acid base disturbance. These adaptations are likely responsible for the enhanced vascular reactivity that may aggravate the patient's clinical status and increase the complication rate during cordocentesis.

The primary central nervous system effect of mild placental dysfunction is delayed maturation of several fetal behaviours. Likewise, the development of autonomic reflexes superimposed on intrinsic cardiac activity determines the characteristics of the fetal heart rate. These reflexes originate in the brain stem and are modulated by the ambient oxygen tension, signals from higher brain centres, the reticular activating system, and peripheral sensory inputs.

Once organized behavioural states are established (typically by 28 weeks gestation), diurnal and responsive cyclicity (eg to maternal glucose) and their coupling to heart rate variation (heart rate reactivity) are usually achieved.

A delay occurs in all aspects of central nervous system maturation in fetuses with IUGR and chronic hypoxemia.

Hypoxemia stimulated erythropoetin release increases red blood cell mass through both medullary and extra medullary haematopoiesis. Placental platelet aggregation and consumption increases the risk of thrombocytopenia.

Fetal Decompesation :

If placental dysfunction is progressive or sustained, the adaptive mechanisms become exhausted and decompensation begins. Metabolic abnormalities are exaggerated, acidemia worsens, and the risk of intra uterine damage or perinatal death increase dramatically.

Forward blood flow in the venous system is determined by cardiac compliance, contractility and afterload. The normal venous flow velocity waveform is triphasic and therefore more complex than the arterial wave forms. It consists of systolic and diastolic peaks (S.wave and D.wave) that are generated by the descent of the arterio ventricular ring during ventricular systole and passive diastolic ventricular filling, respectively.

The sudden increase in right atrial pressure with atrial contraction in late diastolic causes a variable amount of reverse flow producing a second trough after the D-wave (A wave). A decrease in forward cardiac function marks the onset of cardiovascular decompensation and causes decreased forward velocity during atrial systole (A wave)

Impaired preload handling is documented in the precordial veins (ductus venosus, IVC, SVC) hepatic veins and head and neck veins (jugular veins and cerebral transverse sinus). If the failure to accommodate preload is progressive, umbilical venous pulsation may be the ultimate reflection of increased central venous pressure.

Progressive metabolic acidemia is associated with oligoaminos and loss of fetal breathing movement and tone. Abnormal fetal heart rate patterns including overt late decelerations or a decrease in the short term variation on computerized analysis develop and appear to be related to metabolic status and concurrent worsening of cardiac functions.

In the final stages of compromise cardiac dilation with holosystolic tricuspid insufficiency, complete fetal inactivity and spontaneous late decelerations may be seen before intrauterine demise.

<u>Prediction and Screening option for fetal growth restriction</u>

History:

As outlined above, several risk factors can be identified at booking such as BMI < 19 and maternal smoking.

Past history of IUGR increases the risk of recurrence in subsequent pregnancies.

Patients with significant medical or obstetric history such as chronic hypertension, severe toxemia of pregnancy, chronic renal disease and advanced insulins dependant diabetes are at high risk of having IUGR fetuses.

Clinical Examination :

Includes assessment of maternal weight gain and uterine fundal height.

Weight gain : IUGR is suspected in women of average or low weight, with lack of weight gain throughout pregnancy or arrested weight gain after 28 weeks. Chesley reported that the average total weight gain in pregnancy was about 11kgs. During the first trimester the average gain was 1 kg, compared to about 5 kg (0.5 kg / week) during each of the last two trimesters. If the weight gain is below 6 kg, IUGR is likely.

Uterine fundal height :

Uterine fundal height measured from xiphisternum to pubic symphysis in cm along the midline abdomen increases by 1cm / week during 14-32 weeks and later 0.5 cm / week, corresponding to gestational age in weeks from 18-30 weeks. Fundal height discrepancy of more than 2 weeks on successive prenatal visits is suggestive of IUGR.

Maternal serum screening :

Low levels of first trimester PAPP- A levels, low levels of second trimester alpha fetoprotein, oestriol (E3), human placental lactogen (HPL), human chorionic gonadotrophin, inhibin A have shown a less consistent picture.

Ultrasound assessment :

Sonographic measurements of the fetus provide information about fetal age and growth. These data are used to assign gestational age, estimated fetal weight and diagnose growth disturbances.

Fetal Head measurements

These measurements involve the fetal head BPD, corrected BPD and HC. All three measurements are taken from transaxial sonograms of the fetal head at the level of the paired thalami and cavum septi pellucidi.

Corrected BPD :$\sqrt{}$ (BPD x OFD) / 1.265

Although BPD is simpler to measure than the corrected BPD or HC it has the disadvantage of being the only one of the three measurements that disregards head shape. In patients with asymmetric IUGR, BPD may not identify IUGR

Femur length :

The length of the diaphysis of the fetal femur is often used. It may be affected relatively very late.

Abdominal circumference :

The fetal AC is the length of the outer perimeter of the fetal abdomen measured on transverse scan at the level of the stomach and intrahepatic portion of the umbilical vein.

AC is decreased in both symmetric and asymmetric IUGR.

Transverse cerebellar diameter :

It has been suggested as an indicator of gestational age when dates are uncertain and their growth parameter are suspected of lagging behind.

Head to abdomen ratio :

This ratio compares the most preserved organ in the malnourished fetus, the brain, represented by the circumference of the fetal head, with the most compromised organ, the liver represented by the fetal AC. This measurement is of significant value in identifying FGR babies with asymmetric head to abdomen measurements.

Femur to abdomen ratio :

This method compares the FL which is minimally affected by fetal growth impairment with the AC which is the most affected. The femur to abdomen ratio remains constant after 20 weeks.

The normal values for this index is 22±2. When the FL/AC ratio is abnormally high, FGR should be strongly suspected.

TCD / AC ratio :

The distance between the outer borders of the cerebellum or transverse cerebellar diameter is not markedly affected in cases of FGR and can be used as index of the gestational age in combination with AC measurements.

The normal TCD / AC ratio is 0.137 ± 0.012.

Fetal ponderal index :

The fetal ponderal index is gestational age independent and has constant value throughout the second part of the pregnancy.

FPI = EFW / (FL)3

Normal value is 8.325 ± 2.5. An FPI of 7.0 or less should be considered abnormal and suggestive of FGR.

Amniotic fluid volume :

It is important in the surveillance of FGR the presence of oligoamnios, defined as the largest umbilical cord free pocket of fluid with diameter < 2cm, suggests severe fetal compromise in FGR pregnancies but is not by itself an indication for delivery.

Placenta :

Mature placenta may occur earlier in gestation when the fetus is either stressed or growth retarded. Growth retardation is often associated with decreased placental weight.

Estimated fetal weight :

The determination of EFW is based on accurate ultrasound measurements of four anatomic landmarks BPD, HL, AC, FL. The most commonly used formula to determine EFW and the most commonly used percentile distribution nomograms are from Hadlock et al (1984, 1991).

Ultrasonic fetal weight estimates are usually within 5-10% of the true fetal weight. Fetal weight estimates have a sensitivity of 89%, specificity of 88%, positive predictive value of 45% and negative predictive value of 99% for the detection of FGR.

Doppler Ultrasonogram :

The past 20 years have seen an enormous growth in both the technical aspects of Doppler USG and its applications in obstetrics and fetal medicine.

Physical principles of Doppler Ultrasonography

Doppler effect :

The phenomenon of observed changes in the frequency of energy wave transmission when relative motion occurs between source of wave transmission and the observer. The change in the frequency is known as Doppler frequency shift or simply the Doppler shift.

fd = ft – fr where fd is the Doppler shift frequency

ft is the transmitted frequency and

fr is the received frequency

When the source and observer move closer, the wavelength decreases and the frequency increases. Conversely, when the source and the observer move apart, the wavelength increases and the frequency decreases. This principle applies to all forms of wave propogation. The utility of the Doppler effect originates from the fact that the shift in frequency is proportional to the speed of movement between the source and the receiver and therefore can be used to assess this speed.

Doppler ultrasound :

The phenomenon of the Doppler effect is also observed when an ultrasound beam encounters blood flow. With blood circulation millions of red blood cells act as moving scatterers of the incident ultrasound. In this circumstance like erythrocytes act first as moving receiver and then as moving sources forming the basis for the Doppler equation.

$fd = 2\ ft\ \ V/C$ where fd represents the Doppler frequency shift,

ft is the frequency of incident beam (transducers frequency)

V the velocity of scatterer in a given direction

L is the propogation speed of sound in the medium

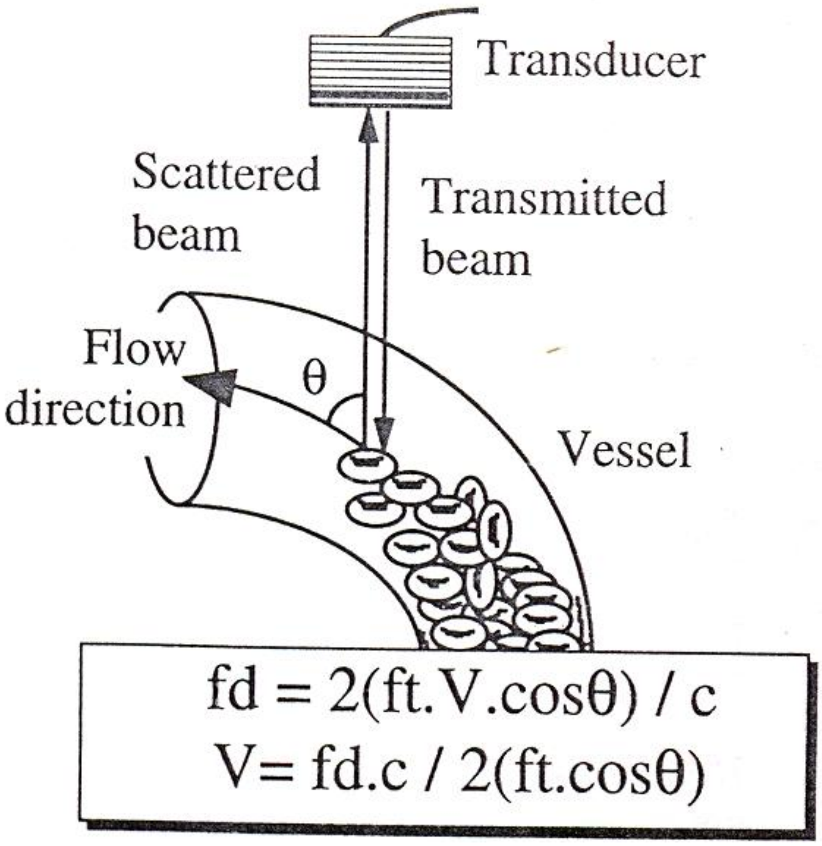


FIG. DOPPLER EFFECT WHEN USG BEAM INTERROGATES CIIRCULATING BLOOD

If the direction of the incident beam is at an angle to the direction of blood flow,the v in the Doppler equation is replaced by the component of the velocity in the direction of the flow (obtained by the cosine of angle cos θ)

$$fd = 2ft \cos V / \cos \theta$$

To determine velocity of scatterer the equation can be rewritten as follows.

$$V = fd \; c / 2ft \; \mathrm{Cos}\, \theta$$

Thus, if the angle of beam incidence and the Doppler shift are known, the velocity of blood flow is also known, assuming that the transducer frequency and the velocity of sound in tissue remain relatively constant. The above equation forms the basis for clinical application of the Doppler principle.

High pass and low pass filtering :

Two types of filters are used

a) High pass filter

b) Low pass filter

The purpose of high pass filter system is to eliminate the extrinsic low frequency component of Doppler signals, which arise predominantly from the vessel wall or other adjacent slow moving structures. This should be used with caution as a high setting eliminates end diastolic frequency shifts from umbilical or uteroplacental circulation.

Technical Considerations :

Four types of devices used to obtain Doppler signals are

a) Continuous wave Doppler :

It is relatively inexpensive. This machine has two crystals, one that transmits high frequency sound wave and another that continuously receives signals. It can record high frequencies using low power output and is easy to use. Unfortunately it is non selective and recognizes all signals along its path and does not allow visualization of blood vessels of interests. It is useful to detect fetal heart movements or even umbilical artery pulsation.

b) Pulsed Doppler :

By contrast, pulsed Doppler ultrasound is used to assess flow velocity patterns within arteries and veins that are simultaneously visualized by gray scale ultrasound. Pulsed Doppler gate size, pulsed repetition frequency, angle of isonation and gray scale image (PRF) can be adjusted to obtain pure waveforms of high quality.

In general, blood flow velocities in the placental and fetal circulations range between 10 to 80 cm/sec. Pulsed Doppler is particularly helpful in obtaining reliable uterine artery Doppler waveforms and is essential for assessing various parts of the fetal circulation.

Colour flow Doppler :

Colour flow Doppler is an extension of pulsed Doppler in that a colour signal is assigned to the direction of flow, by convention, red flow towards the probe and blue flows away from it. Colour flow

Doppler, therefore, detects blood flow velocity in the same plane as the ultrasound probe.

Low angles of insonation are required in order that flow may be visualized in various vessels. Flow is best observed at appropriate PRF settings. Otherwise no flow may be detected or a multitude of low flow vessels will obscure the vessels of interest.

Power Doppler :

Recent technical development that detects blood flow velocity independent of the angle of isonation. This method of imaging is particularly useful in assessing areas of high blood flow velocity and in delineating vascular from non vascular areas.

Wave form Analysis :

Quantitative Analysis :

The Doppler output results in the flow velocity waveform (FVW) representing the velocity envelope through the cardiac cycle. There are three common methods of describing peak blood flow velocity wave forms.

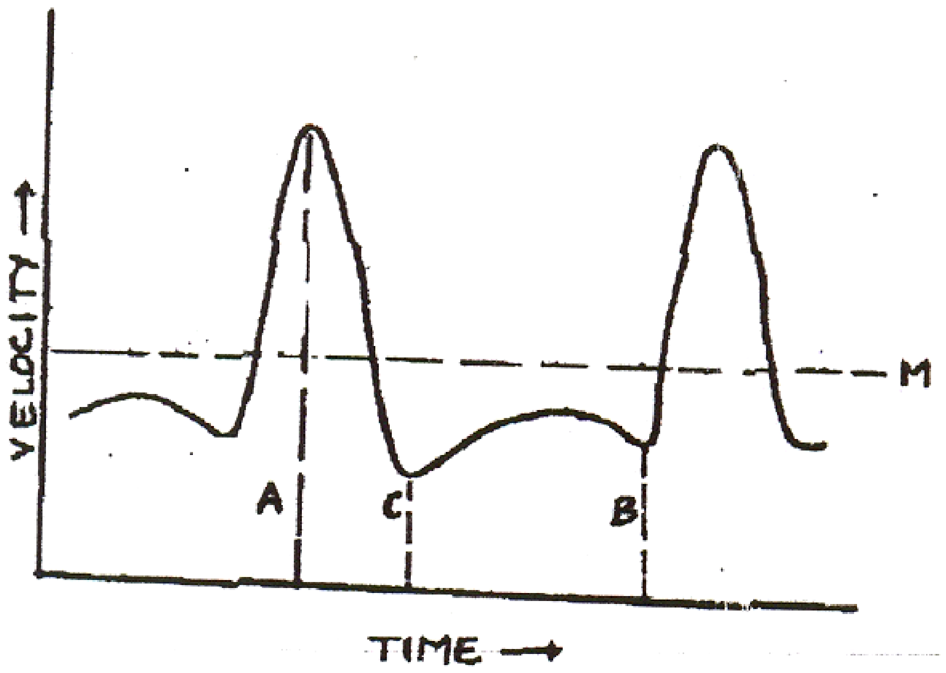


FIG.TYPICAL WAVEFORM

1. Systolic / Diastolic ratio $= \dfrac{\text{Peak systolic velocity}}{\text{End diastolic velocity}} = A/B$

2. Pulsatility Index $= \dfrac{\text{Peak systolic - End diastolic velocity}}{\text{Mean velocity}}$

$$= A – B / M$$

3. Resistance Index (RI) $= \dfrac{\text{Peak systolic - End Diastolic Velocity}}{\text{Peak systolic velocity}}$

$$= A – B / A$$

A- Peak systolic velocity

B - End diastolic velocity

C - Early diastolic velocity

M - Mean velocity

S/D ratio gives a simple evaluation of blood flow during diastole and provides estimation of down stream resistance.

The puslatility index considers the mean velocity as diameter (ie.) the whole of the flow is given consideration, not just the diastolic flow and hence can be used to analyse data from various vessels without encountering the excessive variation that can be caused by duration by small numbers as with other indices.

The pourcelot index or RI is useful when the diastolic flow is absent or reversed and S/D cannot be calculated. It helps in comparing any waveform irrespective of its diastolic flow.

Qualitative Analysis :

Qualitative or descriptive methods may be used to describe wave forms in the uterine, umbilical or middle cerebral artery circulation.

An abnormal uterine artery waveform may be described either by the presence or absence of an early diastolic notch or by the PI.

Umbilical and middle cerebral artery Doppler waveforms may be described as normal with reduced diastolic flow, absent end diastolic flow (EDF) or reversed EDF.

Uterine artery :

In the first half of pregnancy, trophoblasts invade the uterine vessels and result in dilated spiral arteries, which increase the uterine perfusion 10 fold to 12 fold. These arteries provide nutrient supply and gas exchange for the fetus.

The uterine arterial blood flow in nonpregnant women is 50ml/ min and increases to over 700 ml / min in the third trimester of pregnancy. Thus the diastolic component of the uterine artery Doppler in transformed during normal pregnancy from one of low peak flow velocity and an early diastolic notch to one of high flow velocity and absence of early diastolic notch by 18 – 22 weeks.

The uterine artery waveform by the mid – second trimester is therefore characterized by high end diastolic velocities with continuous forward blood flow throughout diastole. With advancing gestation, the degree of end diastolic flow typically increase. Indices used to quantify these waveforms include PI, RI and notching of one or both uterine arteries.

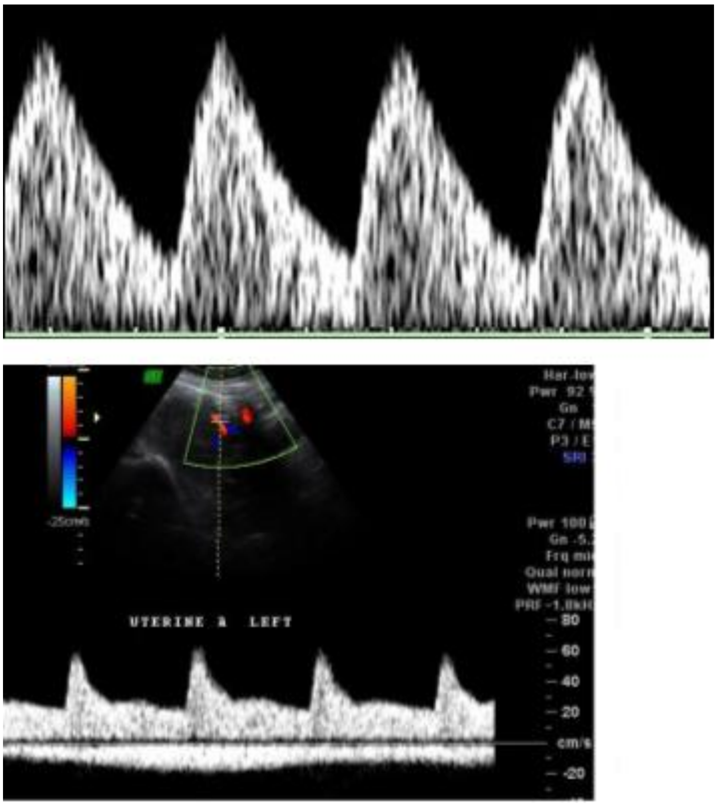


FIG.1-NORMAL UTERINE DOPPLER

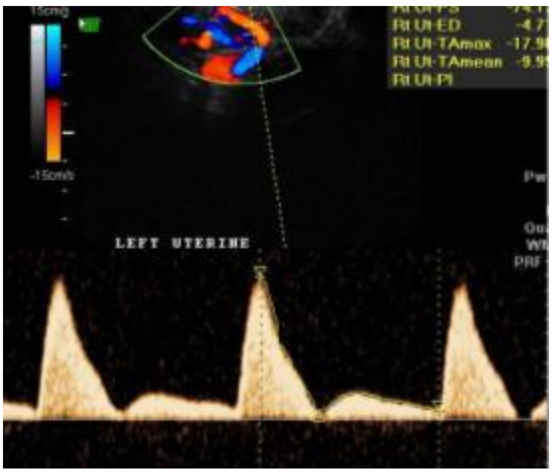


FIG.2.ABNORMAL UTERINE ARTERY

However, failure of normal endovascular trophoblastic invasion of the spiral arteries results in increased uterine artery vascular resistance and decreased perfusion of the placenta. If the end diastolic flow does not increase throughout pregnancy or if a small notch is detected at the beginning of diastole, the fetus is at high risk for developing IUGR. Diastolic blood flow may be absent or even reversed with extreme degree of placental dysfunction.

The PI of each uterine artery should be obtained independently using a PI values of 1.41 to differentiate between normal and abnormal values.

A recent literature review reported that abnormal uterine artery waveforms are a better predictor of preeclampsia than of IUGR when performed after 16 weeks gestation. However different induces best predicted preeclampsia or IUGR based on the a prior risk. Thus, an abnormal PI and uterine artery notching in the second trimester best predicted pre eclampsia, whereas the best predictor of IUGR was an increased RI

The indications for the assessment of the uterine artery Doppler ultrasound are

1. Previous history of pre – eclampsia
2. Previous child with IUGR
3. Unexplained high maternal serum alpha FP
4. High human chorionic gonadotropin levels.

If the PI values of both uterine arteries is normal, the patient can be informed that she most likely will not develop preeclampsia or have an IUGR fetus. This is because of the high negative predictive value (>99%) of the test. If one of the uterine arteries is abnormal patients are followed with more frequent clinic visits and ultra sounds for growth because the positive predictive value in populations at risk ranges from 50% to 75%.

Umbilical Artery :

The UA Doppler indicates the presence or absence of placental resistance to the blood flow from the fetus to the placenta and has a strong correlation with the acid base balance of the fetus. The measurement of interest is the UA S/D ratio. In European countries the PI is used more frequently than the S/D ratio. The PI has the advantage of producing a numerical value and when diastolic flow is absent.

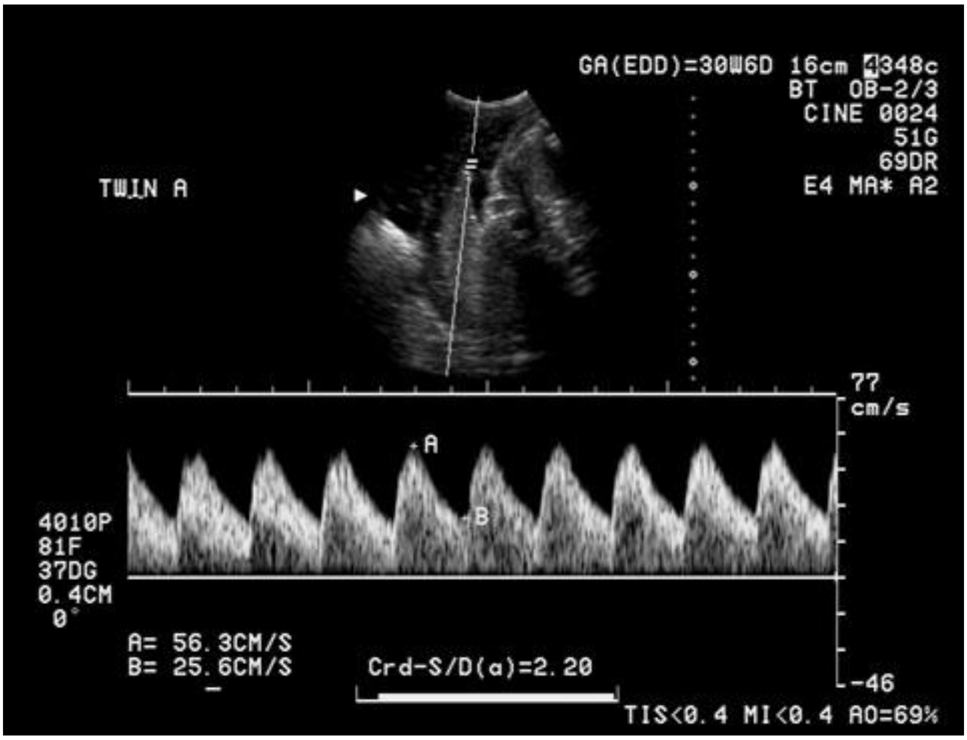


FIG.3.NORMAL UMBILICAL ARTERY DOPPLER

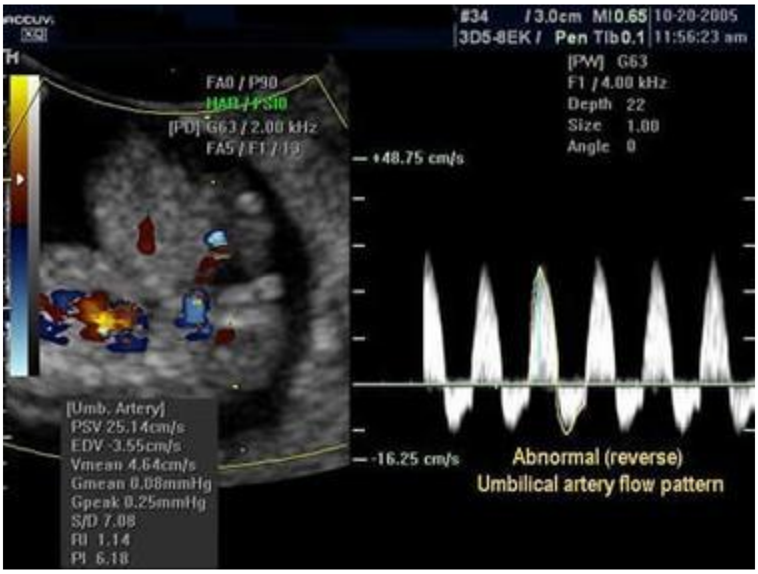


FIG.4.REVERSAL OF UMBILICAL ARTERY

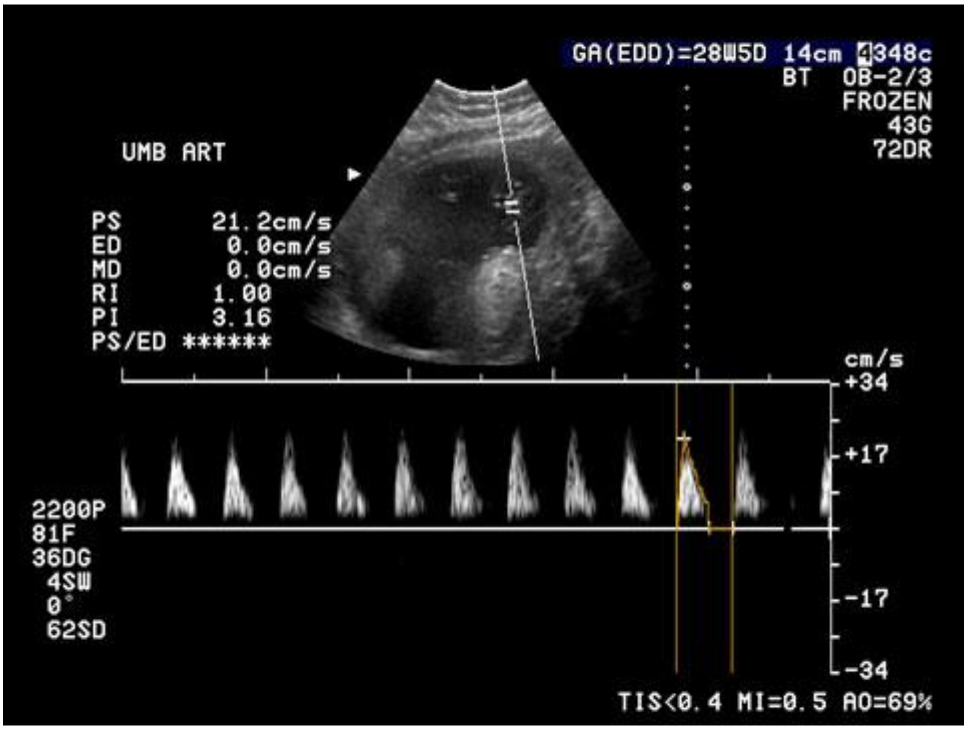


FIG.5.ABSENT DIASTOLIC FLOW IN UMBILICAL ARTERY

Gestation (Weeks)	Hypertensive			Normotensive		
	S/D	RI	PI	S/D	RI	PI
32-34	4.74 ± 1.78	0.94 ± 0.26	2.0 ± 0.82	2.92 ± 0.06	0.65 ± 0.02	1.1 ± 0.14
35-37	3.54 ± 0.97	0.78 ± 0.12	1.27 ± 0.32	2.36 ± 0.09	0.56 ± 0.03	0.77 ± 0.05
38-40	3.09 ± 0.76	0.72 ± 0.11	0.99 ± 0.23	2.23 ± 0.13	0.55 ± 0.02	0.74 ± 0.06

FIG.8.DOPPLER VALUES OF UMBILICAL VESSEL

To obtain more consistent results, the UA S/D ratio should be obtained in a free loop of cord midway between the placental insertion, the site of less resistance and the fetal insertion, the site of maximal resistance flow.

During normal pregnancy the UAs have low resistance demonstrated by the presence of abundant diastolic flow and reflected in low S/D ratios. During normal pregnancy there is a slow and continuous decline in the S/D ratio that reaches it lowest value after 36 weeks gestation.

When the pregnancy is complicated by increased placental vascular insufficiency causing FGR, diastolic flow decreases causing the UA S/D ratio to increase to values 2SD or higher above the mean for the gestational age. An increase in UA S/D ratio even if it is marked is not an indication of fetal hypoxemia or acidosis. However, with the progression of placental vascular insufficiency the UA waveforms will show ADF and finally reversed diastolic flow (RDF) which indicate the presence of fetal hypoxemia and the need to deliver the fetus.

Randomised clinical trials and meta analysis have demonstrated that the use of UA Doppler in high risk pregnancies results in an approximately one third decrease in perinatal mortality (Alfirevic and Neilson 1995 ; Divon 1996, Goffinet et al 1997).

Studies have also demonstrated strong relationship between the results of UA velocimetry and the presence of fetal acedemia in blood sample obtained by cordocentesis (Vintzileous et al 1991 ; Yoon et al 1993).

Middle Cerebral Artery :

When the placental vascular resistance increases above a certain threshold, the fetus develops a compensatory response, increasing the blood flow to vital organs such as the heart and the brain and decreasing the blood flow to the mesenteric, renal and peripheral circulations. This hemodynamic adaptation protects the integrity of the fetal brain in the face of diminished availability of nutrients and can be assessed by comparing the UA and MCA Doppler waveforms.

Under normal conditions, the UA waveforms are characterized by abundant diastolic flow corresponding to a minimal resistance to flow in the fetal placental circulation. The MCA waveforms are completely different and show minimal or no diastolic flow indicating high resistance to flow.

During the initial stages of placental insufficiency the UA diastolic flow decreased and the S/D ratio increases while the compensatory increase of the brain circulation causes increase in diastolic flow with resulting decrease in the MCA S/D ratio. With progression of placental insufficiency, the UA and MCA S/D ratios become similar and eventually the MCA S/D ratio will become smaller than the UA S/D ratio. This is called ‘Brain sparing effect’ or ‘centralization’ of flow.

Centralization is a signal that the fetus is under appreciable placental resistance to flow and inadequately compensating for this problem by improving the blood flow to the brain.

In one of the first studies on his subjects Arduim et al (1987) studied 75 patients at risk for having growth restricted babies. Of them 53% had hypertension, 24% were heavy smokers, 14.7% had a history of malnourished fetuses and 8% had renal disease. The study was done at 26-28 weeks of gestation and before any of the fetuses exhibited ultrasonic signs of growth impairment. At birth, 52 neonates (69.3%) had normal birth weights and 23 (30.7%) were small and had signs of malnutrition. According to these investigators, the ratio between the PI of the fetal umbilical and carotid arteries predicted the occurrence of fetal malnutrition with a specificity of 92.3%, a sensitivity of 78.2% and positive and negative predictive values of 81.8% and 91.5% respectively. Other investigators have found that a UA / MCA ratio < 1.0 identifies the fetuses at risk of FGR and poor neonatal outcome.

The MCA should be sampled soon after its origin from the internal carotid artery. Reference values for the MCA PI change throughout gestation. The lower PI values early and late in gestation may be caused by the increased metabolic requirements of the brain during these periods. Several conditions are associated with an increase or decrease of the MCA PI when compared to normal value.

The MCA PSV is increased in IUGR fetuses. This increase predicts perinatal mortality more accurately than does the MCA PI. This finding can be explained because initially the MCA PI is abnormal in most IUGR fetuses but subsequently increases and trends towards normalization before delivery or fetal death. Conversely, the MCA PSV progressively increases with advancing gestation in all fetuses and tends to decrease slightly just before fetal biophysical deterioration or fetal demise. Despite this decrease, however the MCA PSV values remains above the upperlimit of normal until a few hours before delivery or fetal demise.

Although the MCA PSV is increased in anemic fetuses, those with IUGR are not anemic raising the question, what is the mechanism of increased MCA PSV in anaemic and non anemic fetuses? Hanif et al, showed that the mechanisms determining increased MCA PSV values are different in anemic AGA fetuses compared with nonanemic IUGR fetuses. In anemic fetuses the high

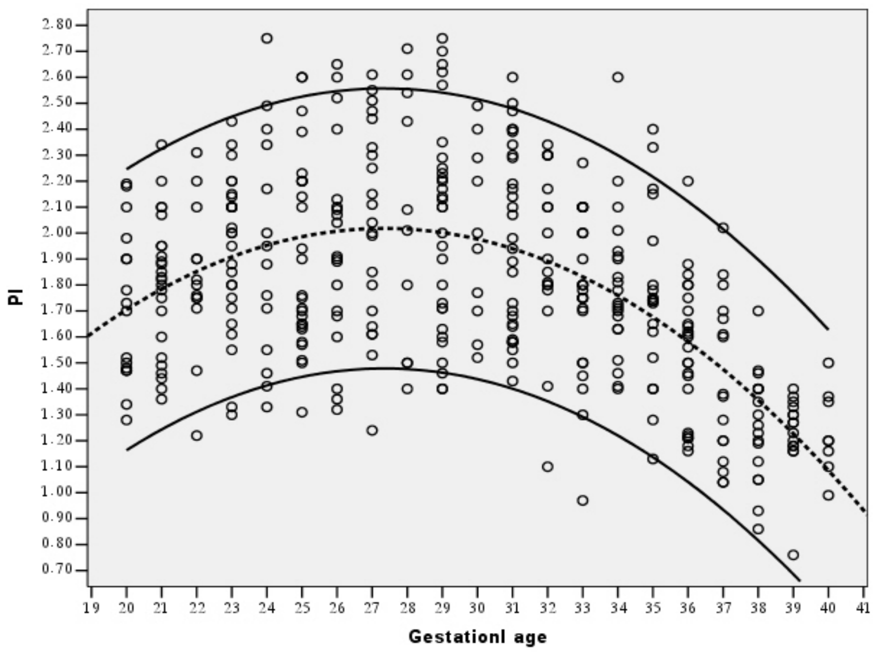


FIG.9.MCA PI FOR CORRESPONDING GESTATION

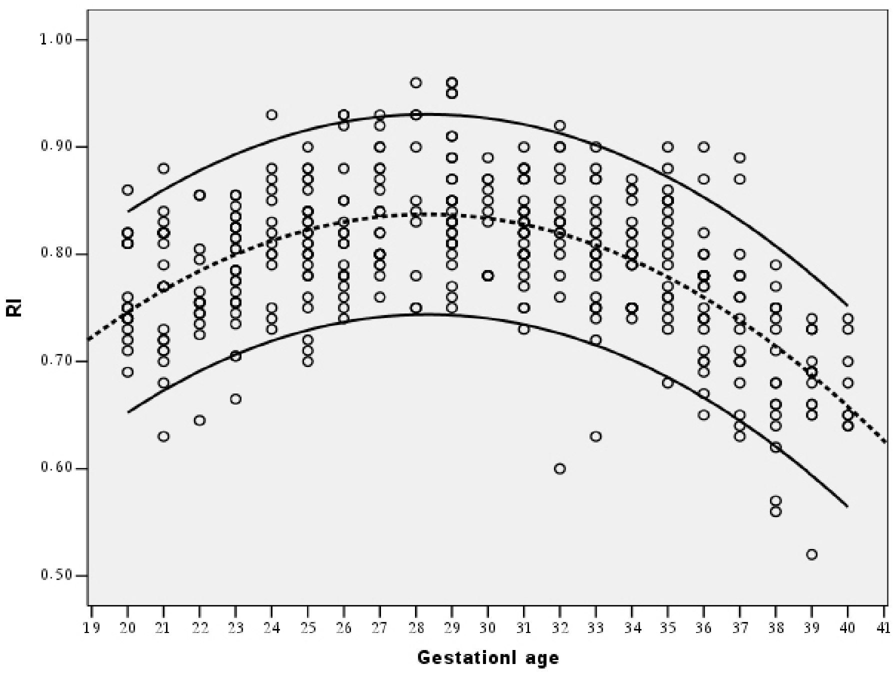


FIG.10.MCA RI FOR CORRESPONDING GESTATION

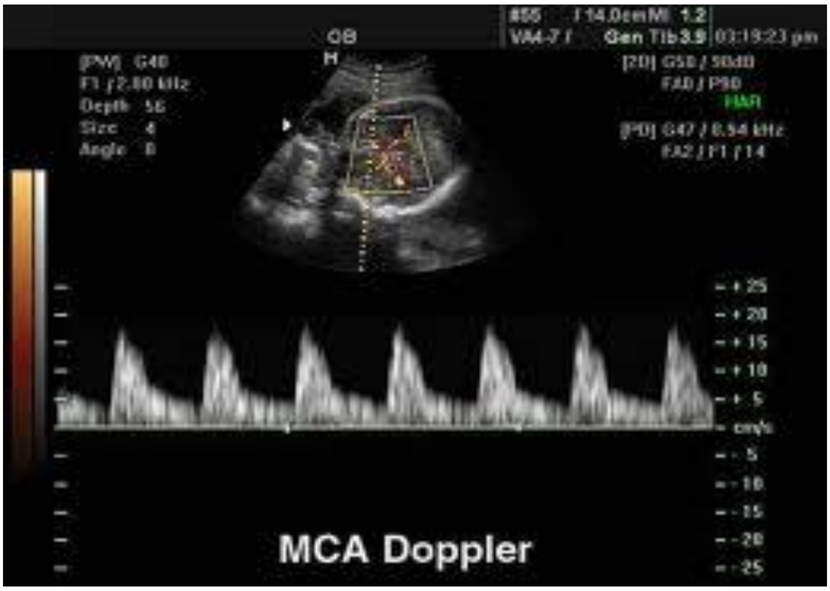


FIG.6.NORMAL MCA DOPPLER

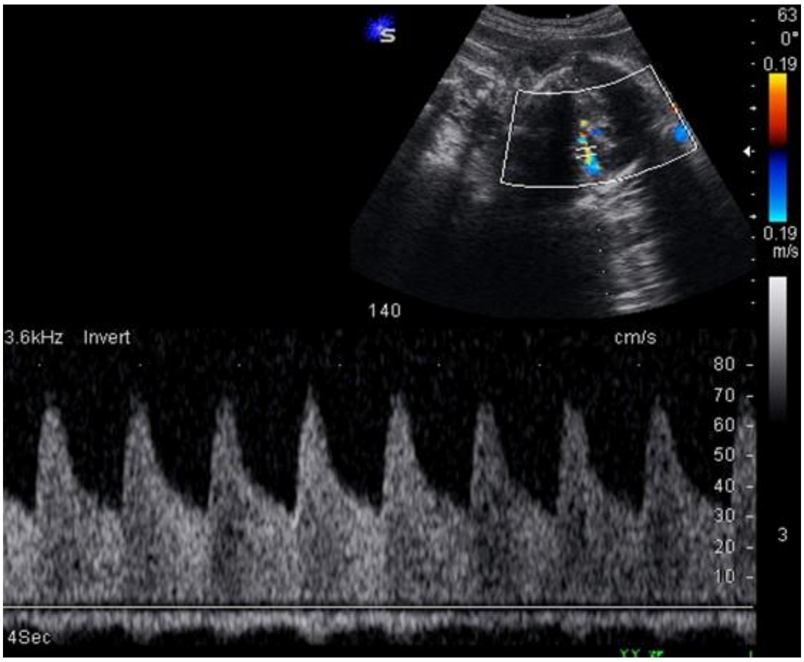


FIG.7.BRAIN SPARING EFFECT OF MCA

MCA PSV is related to a decreased fetal hemogloblin that can decrease blood viscosity, therefore cardiac output increases. In IUGR fetuses, however, the MCA PSV increase in significantly related to hypoxemia and hypercapnia and thus to brain autoregulation.

Other arteries :

Many other arteries like the descending aorta, splenic artery, superior mesenteric artery, adrenal artery, renal artery, femoral, internal iliac and external iliac arteries have been examined in AGA fetuses and those with IUGR, increasing our understanding of fetal physiology and pathophysiology in these conditions. However the study of these vessels as currently performed adds no new information to the study of the UA and MCA in the management of IUGR fetuses.

Fetal Venous system :

Studies on fetal venous blood flow have been performed on the blood flow from the placenta, which returns to the heart through the umbilical vein. Normal flow in the free floating umbilical vein is monophasic. Fetuses with pulsations in the umbilical vein in the second and third trimesters have a higher morbidity and mortality even in the settings of normal UA blood flow.

Doppler Ultrasound staging Guidelines for IUGR

Stage I	-	Abnormal UA PI
		Abnormal MCA PI
Stage II	-	Umbilical artery absent / reversed flow
		Elevated MCA PSV
		Abnormal ductus venosus PI
		Umbilical vein pulsation
Stage III	-	Ductus venosus reversed flow
		Umbilical vein reversed flow
		Tricuspid value (TV) E/A ratio > 1
		Tricuspid valve regurgitation (TR)

Safety of Doppler Ultrasound :

Equipments are regulated to be set for the lowest power settings sufficient to produce adequate images, known as the ALARA (as low as reasonably achievable) principle.

The biologic effect of high energy ultrasound include heating and cavitation of tissues and teratogenicity ,mutagenictiy.

Cavitation :

Caused by the vaccum following the ultrasound pulsed wave and is employed in the noninvasive lithotripsy destruction of kidney stones.

This is never observed in tissues exposed to the low levels of USG energy used in diagnostic USG.

Heating :

Dependent on USG intensity ,duration of exposure and type of tissue. In animal experiments, the effect may increase the fetal brain temperature just below the skull by over 4°C. Neural tissue is particularly sensitive to hyperthermia

Neural tube defects and microcephaly have been observed.

Potential Pit falls :

a) Angle of Insonation :

Common Doppler indices such as PI, RI and S/D ratio are not influenced by the angle of insonation. However, high angles of insonation will reduce the calculated peak velocity such that the proportion of the total wave form attributable to background noise will become greater.

Wide angles of insonation can lead to apparent loss of diastolic frequencies leading to erroneous diagnosis of placental vascular insufficiency.

b) Heart rate :

An increase in the fetal heart rate will shorten the line to diastole and therefore, lead to increased diastolic flow velocities.

Conversely in complete heart block, a long diastolic phase will result in low diastolic velocities and high PI values.

MATERIALS AND METHOD OF STUDY

Study Design :

Prospective Observational study

Source of Data :

This study was carried out in the antenatal cases who delivered at the Department of Obstetrics and Gynaecology, Madurai Medical College, Madurai. Cases were enrolled during the study period from October 2010 to November 2011.

Inclusion Criteria :

All singleton pregnant women irrespective of age or parity complicated by IUGR which is diagnosed either clinically or ultrasonographically.

Exclusion Criteria :

a) Patient with congenital anomaly of fetus

b) Multiple gestation

c) Preterm babies

d) Unreliable LMP or without I trimester scan

Method of study :

In this study, antenatal pregnant women complicated by IUGR were identified and who fulfilled the criteria mentioned above were enrolled as cases. For each case, history as mentioned in the proforma was taken followed by a general, physical, systemic and obstetric examination.

Ultrasound was done in the cases and the following parameters namely fetal biometry, estimated fetal weight, amniotic fluid index and Doppler ultrasound of the umbilical, middle cerebral and uterine artery were noted.

Doppler USG was done with Duplex Doppler system (3.5mHz)

The patient was placed in supine position with left lateral tilt of 15 degree to avoid caval compression.

Uterine Artery :

Uterine artery was examined with the probe kept 3 cm medial to anterior superior iliac spine and directed towards the lateral wall of the uterus. The cross over of the uterine artery and external iliac vessels was identified and the samples site was chosen. Waveforms were recorded from both uterine arteries.

Umbilical artery :

Flow velocity waveforms was recorded from the free floating loops in mid position. The diagnosis of the absent end diastolic flow or reversed end diastolic flow were made when same Doppler patterns was demonstrated in three separate sampling sites.

Middle cerebral artery :

Wave forms are recorded from MCA as it courses through the lateral sulcus. Colour Doppler is used to map the circle of willis.

RESULTS

103 women entered this prospective study over a period of one year. 100 patients delivered at our Hospital, 3 patients were excluded from the study as they did not deliver at GRH. Hence the statistical analysis was done on 100 cases.

103 women (single term pregnancy) – Term pregnancy

↓

103 had scans

↓

100 with known outcome were taken for analysis

Table – 1

Distribution of cases based on age

Age	No.of cases	Percentage(%)
< 20	10	10
20 – 30	77	77
> 30	13	13

77% belonged to age group 20-30 years, 13% were above 30 years and 10% were < 20 years.

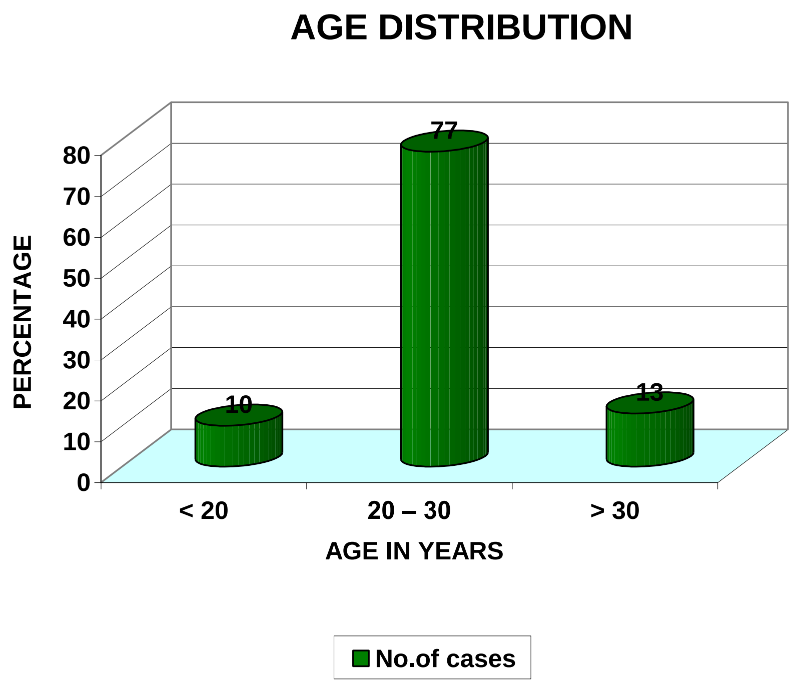

AGE DISTRIBUTION
PERCENTAGE
80
70
60
50
40
30
20
10
0
77
10
13
< 20
20 – 30
> 30
AGE IN YEARS
No.of cases

Table – 2

Distribution of cases based on Parity

Gravida	No.of cases	Percentage(%)
1	46	46
2	32	32
3	18	18
4 and above	4	4

46% of them were primi, and 54% were multipara

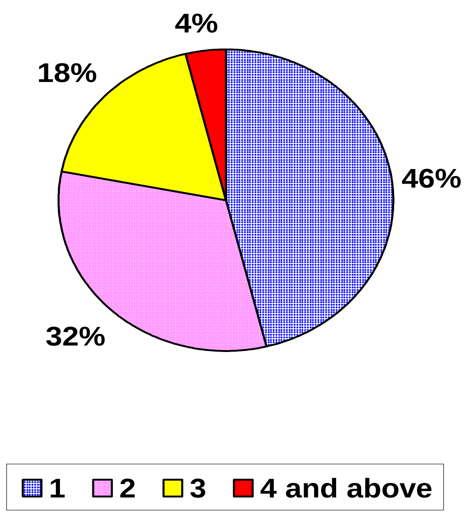
Table – 3

Distribution of cases based on Socio economic status

Socio economic status	No.of cases	Percentage(%)
I	0	0
II	0	0
III	5	5
IV	49	49
V	46	46

49% belonged to class IV socio-economic status, 46% belonged to class V socio-economic status, 5% were of class III socio-economic status.

DISTRIBUTION OF CASES BASED ON PARITY



DISTRIBUTION BASED ON SOCIO ECONOMIC STATUS

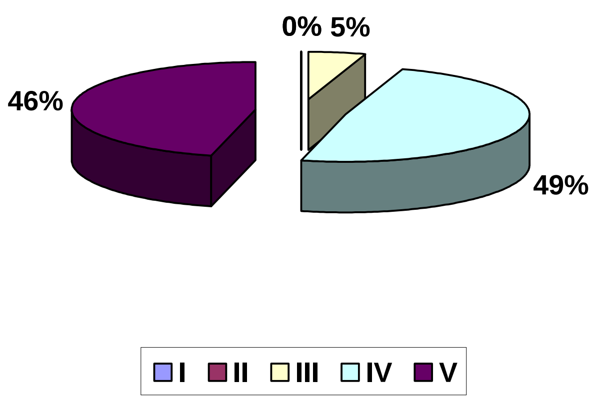


Table – 4

Distribution of cases based on Etiology

Etiology	No.of cases	Percentage(%)
Idiopathic	31	31
Gestational hypertension	34	34
Anemia	11	11
Heart Disease	9	9
Placenta previa	5	5
Chronic maternal disease	7	7
Miscellaneous	3	3
Total	100	100

It is seen that 34% had h/o hypertension on pregnancy whereas 31% had no specific history, 11% had associated anemia.

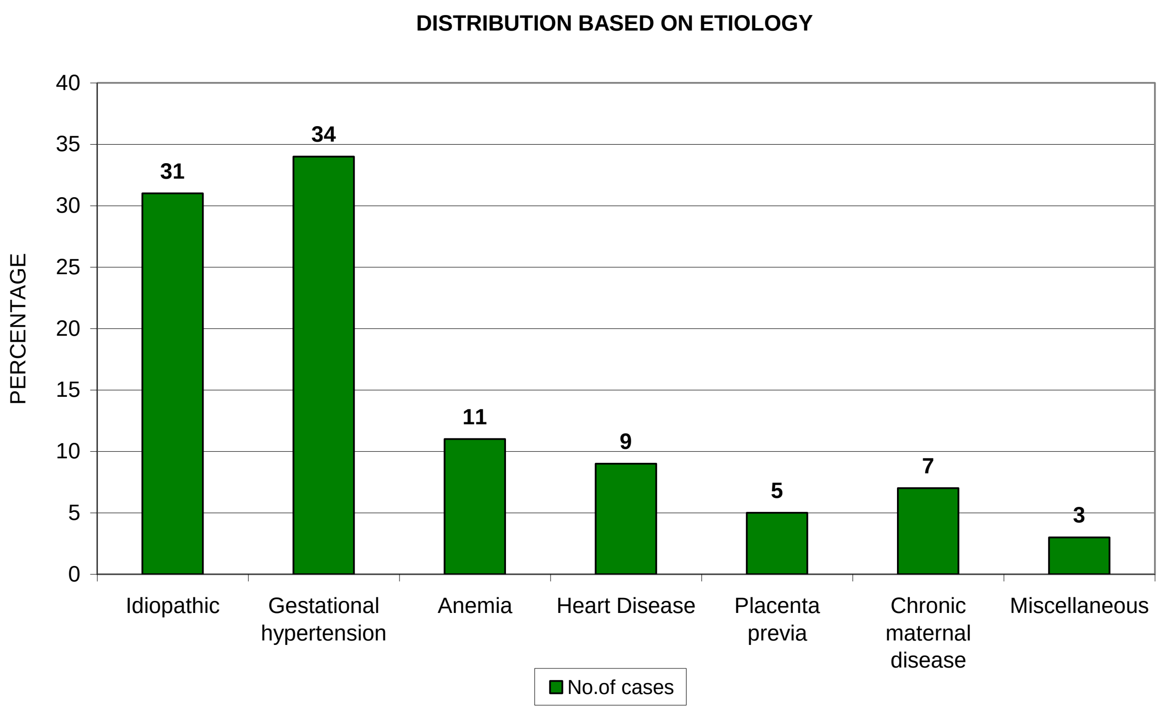

DISTRIBUTION BASED ON ETIOLOGY
PERCENTAGE
40
35
30
25
20
15
10
5
0
31
34
11
9
5
7
3
Idiopathic
Gestational hypertension
Anemia
Heart Disease
Placenta previa
Chronic maternal disease
Miscellaneous
No.of cases

Table – 5

Distribution of cases based on Pregnancy weight gain

Weight gain	No.of cases	Percentage(%)
< 5 kgs	9	9
6 – 10 kgs	71	71
>11 kgs	20	20
Total	100	100

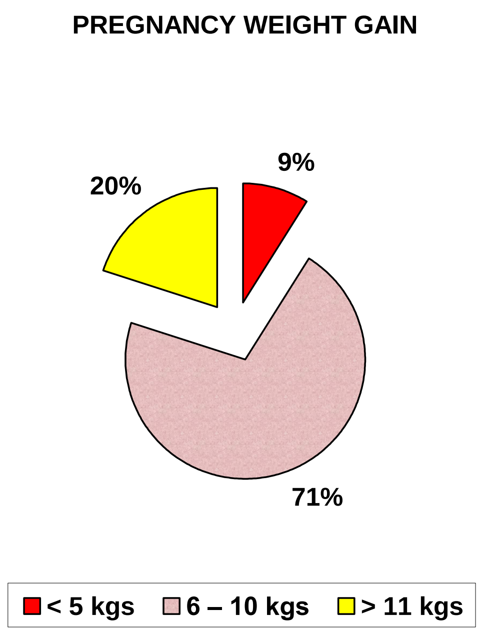
71% had weight gain between 6-10 kgs whereas 20% had weight gain of > 11 kg due to associated preeclampsia, pedal edema, abdomen wall oedema.

Table – 6

Distribution of cases based on AFI

AFI	No.of cases	Percentage(%)
$\leq$ 5	34	34
6 – 10	41	41
11 – 15	19	19
> 15	6	6
Total	100	100

24% had severe oligoamios whereas 41% had reduced liquor.


PREGNANCY WEIGHT GAIN
9%
20%
71%
< 5 kgs
6 – 10 kgs
> 11 kgs

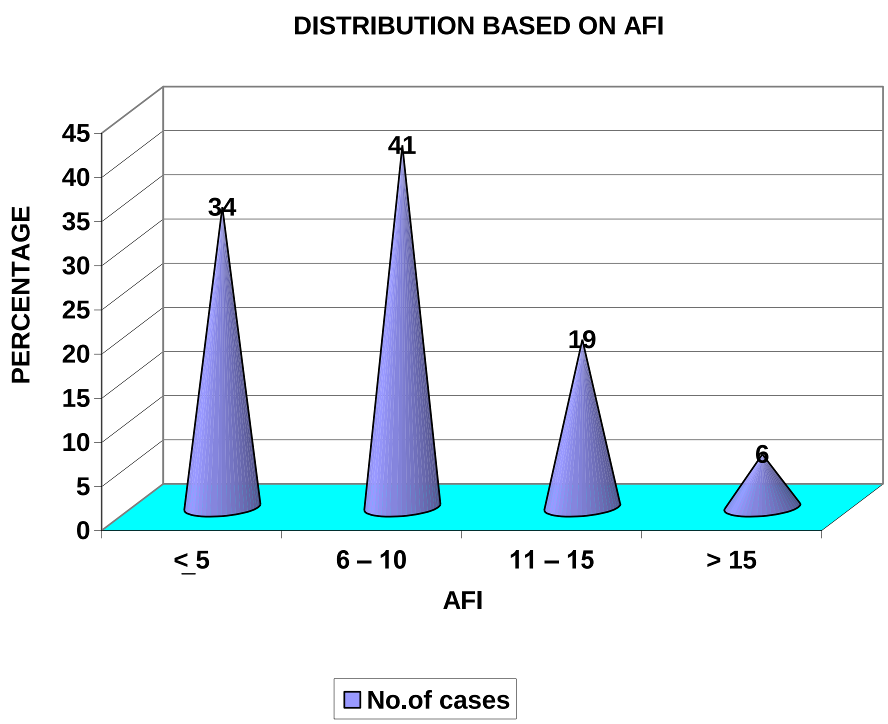

DISTRIBUTION BASED ON AFI
PERCENTAGE
45
40
35
30
25
20
15
10
5
0
34
41
19
6
≤ 5
6 – 10
11 – 15
> 15
AFI
No.of cases

Table – 7

Distribution of cases based on FL / AC

FL/AC	No.of cases	Percentage(%)
Normal	13	13
Abnormal	87	87

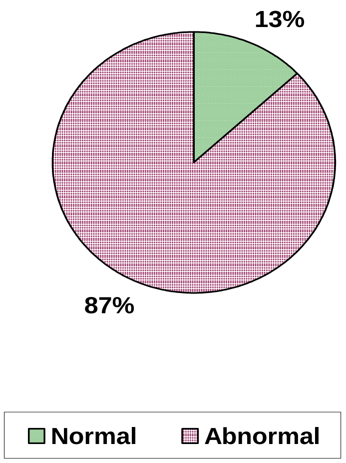
Table – 8

Distribution of cases based on HC/AC

HC / AC	No.of cases	Percentage(%)
Normal	18	18
Abnormal	82	82

It is seen that 13% had normal FL/AC and HL/AC thereby having asymmetrical IUGR. Around 87% had abnormal FL/AC and HC/AC thereby having asymmetrical IUGR.

DISTRIBUTION BASED ON FL / AC



DISTRIBUTION BASED ON HC / AC

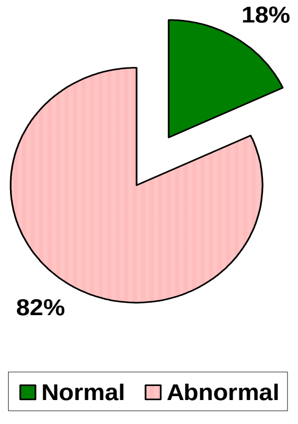


Table – 9

Uterine artery Doppler value distribution and perinatal outcome

Uterine artery Doppler	Perinatal Outcome	
	Normal	Abnormal
Normal (64)	54	10
Abnormal (36)	14	22

Uterine artery Doppler flow was normal is 64%, of those 54 cases (84%) had good perinatal outcome and 16% had abnormal outcome.

Abnormal flow pattern in uterine artery was seen in 36%. 22 of them had abnormal perinatal outcome – 61%. 39% had normal perinatal outcome.

Table – 10

Types of Uterine artery abnormality and associated perinatal outcome.

Doppler flow pattern	Perinatal outcome			
		Abnormal		
	Normal	Total	Mortality	Morbidity
Normal (64)	54	10	3	7
Abnormal (36)	14	22	11	10
U/L high resistance	10	7	1	6
B/L High resistance	6	5	2	3
U/L notch	5	10	4	6
B/L notch	0	3	3	0

Normal uterine artery Doppler flow was associated with 84.3% good perinatal outcome and 15.7% had abnormal outcome. The neonatal mortality was 4.6% and neonatal morbidity was 10%.

When uterine artery was abnormal 38.8% of cases had good perinatal outcome, 61.2% had abnormal outcome, perinatal mortality being 30.5%.

High impedence flow in single uterine artery was associated with abnormal outcome in 41.1% of cases, mortality being 5%.

High resistance flow in both uterine artery was associated with abnormal outcome in 41.6% of cases and 16% was the mortality rate.

Notching of one of the uterine artery had 66.6% abnormal perinatal outcome, 26.6% was the perinatal mortality.

Bilateral notch was associated with 100% mortality.

This shows bilateral uterine artery abnormality to be more significant than unilateral abnormality in predicting abnormal perinatal outcome, the mortality being 100% with bilateral notch.

Table – 11

Umbilical artery Doppler value distribution and perinatal outcome

Uterine artery Doppler	Perinatal Outcome	
	Normal	Abnormal
Normal (76)	68	8
Abnormal (24)	5	19

Umbilical artery flow pattern was normal in 76% of cases, out of these 10% had abnormal perinatal outcome.

Abnormal umbilical artery flow was see in 24% of cases, out of which 79% had abnormal perinatal outcome.

Table – 12

Types of Umbilical artery abnormality and associated perinatal outcome

Umbilical artery Doppler	Perinatal outcome			
		Abnormal		
	Normal	Total	Mortality	Morbidity
Normal (76)	68	8	4	4
Abnormal (24)	5	19	15	4
High resistance (17)	5	12	6	6
AEDF (6)	0	6	6	0
RDF (8)	0	8	8	0

When umbilical artery flow was normal 89.4% had good perinatal outcome with only 10.6% having adverse perinatal outcome with equal mortality and morbidity.

Abnormal umbilical artery flow was associated with 79.1% having abnormal perinatal outcome, mortality being 62.5%.

High resistance flow in umbilical artery showed 70.5% having poor perinatal outcome and equal rate of morbidity and mortality.

AEDF and RDF in umbilical artery is associated with 100% mortality.

Table – 13

Middle cerebral artery Doppler value distribution and perinatal outcome

MCA Doppler	Perinatal Outcome	
	Normal	Abnormal
Normal (86)	78	8
Abnormal (14)	0	14

MCA Doppler flow pattern was normal is 86% of cases, out of which 90.6% had good perinatal outcome.

Abnormal MCA Doppler flow pattern was seen in 14% cases, out of which 100% had abnormal perinatal outcome.

Table – 14

Distribution of cases based on type of Delivery

Type of delivery	Number	Percentage(%)
Vaginal	33	33
Assisted vaginal	7	7
LSCS	60	60

60% of cases were delivered by LSCS, 33% by vaginal delivery and remaining 7% by assisted vaginal delivery.

Table – 15

Correlation of Uterine artery Doppler with pregnancy outcome

Uterine artery Doppler	Pre eclampsia	IUGR	NICU admission
S/D ratio	33	33	22
RI	29	29	14
Early diastolic notch	38	38	25

38% patients developed preeclampsia

38% developed IUGR

25% required NICU admission

This indicates that notch in uterine artery is associated with poor pregnancy outcome.

Table –16

Correlation of Umbilical artery Doppler with pregnancy outcome

Umbilical artery Doppler	Pre eclampsia	IUGR	NICU admission
S/D ratio	60	40	40
RI	13	25	12
Absent diastolic flow	100	100	0

When umbilical artery Doppler was abnormal

60% patients developed preeclampsia

40% developed IUGR

40% required NICU admission

This indicates that absent diastolic flow is associated with poor perinatal outcome.

Table – 17

Descriptive Statistics for Birth weight, Apgar and stay in NICU

Study variable	No.of subjects	Min	Max
Birth weight	100	0.7	2.6
Apgar 1’	100	0	6
Apgar 5’	100	0	8
Stay in NICU	100	1	45

Minimum number of NICU stay was 1 day and max number of NICU stay was 45 days because of respiratory distress, meconium aspiration syndrome sepsis.

Minimum birth weight was 700 gms and maximum birth weight was 2.6kgs.

Table – 18

Statistical significance of Doppler studies

Uterine Artery studies

Uterine Artery	Perinatal Outcome	
	Abnormal	Normal
Abnormal (36)	22 (a)	14 (b)
Normal (64)	10 (c)	54 (d)
Total	a+c = 32	b+d = 68

Sensitivity $\dfrac{a}{a+c} \times 100 = \dfrac{22 \times 100}{32} = 68.75\%$

Specificity $\dfrac{d}{b+d} \times 100 = \dfrac{54 \times 100}{68} = 54.68\%$

Positive predictive value = $\dfrac{a}{a+b} \times 100 = \dfrac{22}{36} \times 100 = 61.1\%$

Negative predictive value = $\dfrac{d}{c+d} \times 100 = \dfrac{54}{64} \times 100 = 84.37\%$

$$\text{Percentage of false (+ve)} = \frac{b}{a+b} \times 100 = \frac{14}{36} \times 100 = 38.8\%$$

$$\text{Percentage of false (-ve)} = \frac{c}{a+c} \times 100 = \frac{10}{32} \times 100 = 31.25\%$$

'p' value = < 0.001 Significant

The above study shows uterine artery Doppler study has statistically significant role in predicting adverse perinatal outcome.

Table - 19

Umbilical Artery studies

Umbilical Artery	Perinatal Outcome	
	Abnormal	Normal
Abnormal (24)	19 (a)	5 (b)
Normal (76)	8 (c)	68 (d)
Total	a+c = 27	b+d = 73

Sensitivity $\frac{a}{a + c} \times 100 = \frac{19 \times 100}{27} = 70.37\%$

Specificity $\frac{d}{b + d} \times 100 = \frac{68 \times 100}{73} = 93.15\%$

Positive predictive value = $\frac{a}{a+b} \times 100 = \frac{19}{24} \times 100 = 79.16\%$

Negative predictive value = $\frac{d}{c+d} \times 100 = \frac{68}{76} \times 100 = 89.47\%$

Percentage of false (+ve) = $\frac{b}{a+b} \times 100 = \frac{5}{24} \times 100 = 20.83\%$

$$\text{Percentage of false (-ve)} = \frac{c}{a+c} \times 100 = \frac{8}{27} \times 100 = 29.62\%$$

‘p’ value = < 0.001 Significant

The above study shows umbilical artery study has to be statistically significant role in predicting abnormal perinatal outcome.

MCA studies

MCA Values	Perinatal Outcome	
	Abnormal	Normal
Abnormal (14)	14 (a)	0 (b)
Normal (86)	8 (c)	78 (d)
Total	a+c = 22	b+d = 78

$$\text{Sensitivity} = \frac{a}{a + c} \times 100 = \frac{14 \times 100}{22} = 63.63\%$$

$$\text{Specificity} = \frac{d}{b + d} \times 100 = \frac{78 \times 100}{78} = 100\%$$

$$\text{Positive predictive value} = \frac{a}{a+b} \times 100 = \frac{14}{14} \times 100 = 100\%$$

$$\text{Negative predictive value} = \frac{d}{c+d} \times 100 = \frac{78}{86} \times 100 = 90.69\%$$

$$\text{Percentage of false (+ve)} = \frac{b}{a+b} \times 100 = \frac{100}{14} = 38.8\%$$

$$\text{Percentage of false (-ve)} = \frac{c}{a+c} \times 100 = \frac{8}{22} \times 100 = 36.36\%$$

‘p’ value = < 0.001 Significant

The above study shows MCA study to be significant in predicting abnormal perinatal outcome.

SUMMARY

In this prospective study in a set up of tertiary level care centre, whose inflow, includes Indian women from rural sector, the predictive values of various Doppler indices have been evaluated.

The prevalence of IUGR (less than 10^{th} percentile) was 8% similar to that quoted by North et al 1994, (6.6%).

Among the 100 patients studied 36 patients had abnormal Doppler of uterine artery, with 15 patients having unilateral notch and 3 having bilateral notch.

There were 24 patients with abnormal umbilical artery Doppler, with 6 of them having absent end diastolic flow and 8 having reversal of diastolic flow.

Out of these 100 patients studied, 33 patients developed pre eclampsia. This is similar to the results obtained by Kurdi et al. It is seen that notch in uterine artery is a better predictor of pre eclampsia. This is similar to results by Bower et al 1993, Chan et al 1995 and Antga Rlis et al 2000.

The sensitivity, specificity, positive predictive and negative predictive value of uterine artery in predicting perinatal out come is 68.75%, 54.68%, 61.1% and 84.37%.

This is similar to opinion by Irion et al, North et al and Bower et al.

The sensitivity, specificity, positive and negative predictive value of umbilical artery in predicting perinatal outcome is 70.37%, 93.15%, 79.16% and 89.47%.

This is similar to opinion by Alkension et al and Beathe Dorman et al.

The sensitivity, specificity, positive and negative predictive value of MCA in predicting perinatal outcome is 63.63%, 100%, 100%, and 90.69%.

CONCLUSION

1. IUGR fetuses with abnormal umbilical, middle cerebral and uterine flow velocity are at significantly greater risk than those with normal study.
2. Diastolic notch in uterine artery as a single parameter is better than the individual Doppler indices in uterine artery in predicting pre-eclampsia.
3. Umbilical(AEDF orRDF) and MCA(increased diastolic flow) Doppler abnormality is a better predictor of fetal growth restriction and perinatal outcome.
4. Doppler velocimetry can be an important adjunct to conventional antepartum surveillance tests on patients with IUGR fetuses.
5. Abnormal Doppler alone should not warrant an obstetric intervention if other antepartum surveillance tests are reassuring.
6. Once an abnormal Doppler finding is identified the obstetrician is made well aware of the possible complications that can set in and the delivery should be planned in a tertiary care centre with good neonatal facilities.

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PROFORMA

FETAL DOPPLER STUDY OF UMBILICAL, MCA AND UTERINE ARTERY AS PREDICTORS OF ADVERSE PERINATAL OUTCOME IN FETAL GROWTH RESTRICTION

Case No. :	
Name :	Husband Name :
Age :	Date of Admission:
I.P.No. :	Date of Delivery :
Occupation :	Socio-economic status:
Obs. Code :	Preg. Weight gain :
LMP :	
EDD :	

First trimester scan EDD :

EXAMINATION:

General Examination :

Height :	Breast :
Weight :	Thyroid :
Pulse :	Estimated G.A.:
BP :	Abd. Girth :

Systemic Examination :

CVS :	RS :	CTG :
EFW :	PA :	PV :

Investigations :

Hb % : Urine Albumin:

Bld group and type: Sugar:

Blood sugar : Dep:

Urea : PPTCT:

Creatinine : LFT:

USG :

GA : AFI : EFW :

Placental grading Congenital anomalies

FL / AC HC / AC :

Doppler flow in umbilical artery :

	S.D. Ratio	R.I.	P.I.	Diastolic flow
Right				
Left				

Doppler flow in Middle cerebral artery :

	S.D. Ratio	R.I.	P.I.	Diastolic flow

Doppler flow in uterine artery :

	S.D. Ratio	R.I.	P.I.	Diastolic flow
Right				
Left				

Maternal Outcome :

Mode of Delivery	:	Vaginal
		Assisted Vaginal
		LSCS
		Ind :
Intranatal course and Complications if any	:	

Fetal Outcome :

Live Birth / Still birth / IUD	:
Term / Preterm	:
APGAR 1’	:
5’	:
Baby Weight	:
Length of Baby	:
IUGR (symmetrical / asymmetrical)	
Ponderal Index	:
Neonatal complications if any:	

MASTER CHART

										UTERINE			UMBILICAL				MCA				
S.No.	I.P. NO	AGE	PARITY	S.E.STATUS	ETIOLOGY	WGT.GAIN	AFI	FL/AC	HC/AC	PATTERN	HIGH RESIS.	E.D.N	PATTERN	HIGH RESI	A.E.D.F	R.E.D.F	PATTERN	I.D.F	DELIVERY	COND. ON DELIVERY	NNC
1	17552	2	2	4	2	2	2	2	2	2	3	1	1	1	2	2	1	2	3	3	1
2	17483	2	2	4	2	2	2	2	2	2	3	1	2	2	1	2	1	2	3	3	1
3	17459	2	2	4	2	2	1	2	2	2	1	2	1	1	1	1	2	1	1	3	1
4	17482	2	2	4	2	2	1	2	2	2	2	2	1	1	1	1	1	1	1	3	3
5	17514	2	2	4	2	2	1	2	2	2	2	2	1	1	1	1	1	1	1	3	3
6	17483	2	2	5	6	2	2	2	2	1	2	1	1	1	1	1	2	1	3	3	1
7	16676	2	2	4	3	2	1	2	2	1	1	1	1	1	1	1	1	1	3	3	3
8	16669	2	2	4	2	2	2	2	2	1	2	1	1	1	1	1	1	1	1	3	3
9	15927	2	2	5	4	2	1	2	2	1	1	1	1	2	1	1	1	1	2	2	3
10	19401	2	1	5	1	3	3	1	1	1	1	1	1	1	1	1	1	1	3	3	3
11	19413	2	1	5	1	2	3	1	1	1	1	1	1	1	1	1	1	1	3	3	3
12	19409	2	1	5	2	2	1	1	1	1	1	1	1	1	1	1	1	1	3	3	3
13	19253	2	1	4	1	2	2	1	1	1	1	1	1	1	1	1	1	1	3	3	3
14	17792	2	2	4	4	2	1	2	2	2	2	1	1	2	1	1	1	1	3	3	3
15	17893	2	2	5	5	2	2	2	2	1	1	1	1	2	1	1	1	1	3	3	3
16	18641	2	1	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
17	19192	2	1	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
18	19125	2	1	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
19	15018	2	2	4	3	2	2	2	2	1	1	1	1	1	1	1	1	1	3	3	3
20	15278	1	2	4	3	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3

21	19377	2	1	4	1	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3	3
22	18673	3	1	5	2	3	1	2	2	1	1	1	1	1	1	1	1	1	1	3	3
23	19740	2	1	5	2	3	2	2	2	1	1	1	1	1	1	1	1	1	3	3	3
24	19683	2	1	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
25	19451	2	1	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
26	15033	2	2	4	3	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
27	19374	2	1	5	4	2	3	2	1	1	1	1	1	1	1	1	1	1	2	3	3
28	19021	1	2	5	2	2	2	2	2	2	2	1	1	1	2	1	1	2	3	3	1
29	19101	2	1	5	1	3	4	2	2	1	1	1	1	1	1	1	1	1	3	3	3
30	19157	2	1	5	1	3	3	1	2	1	1	1	1	1	1	1	1	1	1	3	3
31	18214	1	1	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
32	16057	2	2	5	4	2	1	2	2	1	1	1	1	1	1	1	1	1	2	3	3
33	16551	3	2	4	1	2	2	2	2	2	2	1	1	1	1	1	1	1	3	3	3
34	16565	2	2	4	2	2	2	2	2	2	3	2	1	1	1	1	1	1	3	3	3
35	9418	2	2	3	7	3	4	2	2	1	1	1	1	1	1	1	1	1	3	3	3
36	18467	2	1	5	2	2	1	2	1	1	1	1	1	1	1	1	1	1	3	3	3
37	15915	2	2	4	2	2	2	2	2	1	1	1	1	2	1	1	1	1	3	3	3
38	15474	2	2	4	4	2	1	2	2	1	1	1	1	1	1	1	1	1	3	3	3
39	11241	1	2	4	1	3	4	2	2	2	2	1	1	1	1	1	1	1	1	3	3
40	19945	2	1	4	1	2	3	2	1	1	1	1	1	1	1	1	1	1	3	3	3
41	2489	2	1	5	2	1	1	2	2	2	3	2	1	1	1	2	2	2	3	3	2
42	2117	3	1	5	2	1	1	2	2	2	3	2	1	1	1	2	2	2	3	3	1
43	7805	2	1	5	2	1	1	2	2	2	3	2	1	1	1	2	2	2	1	2	1
44	1782	2	1	5	2	1	1	2	2	2	3	2	2	1	1	2	1	1	3	3	1
45	1658	3	1	5	2	1	1	2	2	2	3	2	2	1	1	2	1	1	1	3	1

46	1504	2	1	5	1	1	3	2	2	2	2	1	2	2	1	1	2	2	1	2	1
47	1503	2	1	5	3	1	3	2	2	2	2	1	2	2	1	1	2	2	1	2	1
48	1400	3	1	5	5	2	1	2	2	1	1	1	2	2	1	1	1	1	3	3	2
49	1406	2	1	5	2	2	1	2	2	1	1	1	2	2	1	1	1	1	1	3	2
50	1357	3	1	5	2	2	1	2	2	1	1	1	2	2	1	1	1	1	3	3	2
51	2859	3	2	4	3	2	2	2	2	1	1	1	1	1	1	1	1	1	3	3	3
52	9325	3	2	5	4	3	3	2	2	1	1	1	1	1	1	1	1	1	1	3	3
53	9219	2	2	4	1	3	3	2	2	1	1	1	1	1	1	1	1	1	1	3	3
54	9243	2	2	4	3	2	1	2	2	1	1	1	1	1	1	1	1	1	3	3	3
55	1668	2	2	4	2	3	2	2	2	2	2	1	1	1	1	1	1	1	2	3	3
56	1414	2	2	5	5	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	3
57	9025	2	2	4	1	3	3	2	2	1	1	1	1	1	1	1	1	1	1	3	3
58	19425	2	1	5	1	3	3	2	1	1	1	1	1	1	1	1	1	1	3	3	3
59	18571	2	1	3	6	2	1	2	1	1	1	1	1	1	1	1	1	1	1	1	3
60	1388	2	1	5	2	2	1	2	2	2	3	2	2	2	1	1	2	2	3	3	1
61	18648	2	1	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	1	3	2
62	18181	2	1	3	7	3	4	1	2	1	1	1	1	1	1	1	1	1	1	2	2
63	19246	2	1	5	2	2	1	1	1	1	1	1	1	1	1	1	1	1	3	3	3
64	1408	2	1	5	2	2	1	2	2	2	2	2	1	1	1	1	1	1	3	3	2
65	11241	2	1	4	1	2	2	2	2	2	2	1	1	1	1	1	1	1	3	3	2
66	1668	2	1	4	1	2	2	2	2	2	2	1	1	1	1	1	1	1	3	3	2
67	1657	3	1	5	1	2	3	2	2	2	2	1	1	1	1	1	1	1	3	3	2
68	2025	3	2	4	2	3	2	2	2	2	2	1	1	1	1	1	2	2	3	3	1
69	2103	2	2	4	3	2	2	2	2	1	1	1	2	2	1	1	2	2	3	3	2
70	2080	3	2	5	2	1	2	2	2	2	3	3	2	1	1	2	2	2	3	3	2

71	8713	2	2	4	1	2	4	2	2	1	1	1	1	1	1	1	1	1	3	3	2
72	10155	2	2	4	3	3	1	2	2	1	1	1	1	1	1	1	1	1	3	3	2
73	10354	2	2	5	4	2	1	2	2	1	1	1	1	1	1	1	1	1	2	3	3
74	9951	2	2	5	5	2	2	2	2	1	1	1	1	1	1	1	1	1	3	3	2
75	10302	2	2	5	1	2	2	2	2	1	1	1	1	1	1	1	1	1	3	3	2
76	30133	2	2	4	6	3	3	1	1	1	1	1	1	1	1	1	1	1	3	3	2
77	10800	1	2	4	1	3	3	1	1	1	1	1	1	1	1	1	1	1	3	3	2
78	10328	2	2	5	1	3	3	2	2	1	1	1	1	1	1	1	1	1	1	3	2
79	10428	2	2	4	6	2	1	2	2	1	1	1	1	1	1	1	1	1	3	3	2
80	9943	2	2	4	3	2	4	2	2	1	1	1	1	1	1	1	1	1	3	3	2
81	4007	1	1	5	2	2	1	2	2	1	1	1	2	2	1	1	1	1	1	3	2
82	1047	1	1	3	6	2	1	2	2	1	1	1	2	2	1	1	1	1	1	3	2
83	1402	2	1	5	2	2	1	2	2	1	1	1	2	2	1	1	1	1	3	3	2
84	1414	2	2	4	1	2	2	2	2	1	1	1	1	1	1	1	1	1	3	3	2
85	2952	1	1	5	2	2	1	2	2	2	3	2	2	1	2	1	1	1	1	3	2
86	2873	2	1	5	2	1	1	2	2	2	2	3	2	1	2	1	2	2	3	3	2
87	2072	2	2	5	6	2	2	2	1	2	2	2	2	2	1	1	1	1	2	3	2
88	2205	2	2	5	2	2	2	2	2	2	3	3	2	1	2	1	2	2	3	3	2
89	21194	2	2	4	3	2	3	2	2	2	1	1	1	1	1	1	1	1	3	3	2
90	19966	2	1	4	1	2	3	1	1	1	1	1	1	1	1	1	1	1	3	3	2
91	2542	2	2	5	5	2	2	2	2	1	1	1	1	1	1	1	1	1	3	3	2
92	2916	2	1	5	2	2	1	2	2	2	3	2	2	2	1	1	1	1	1	3	2
93	3027	2	1	5	2	2	1	2	2	2	3	2	2	1	2	1	1	1	3	3	2
94	2509	2	2	4	4	2	2	1	1	1	1	1	1	1	1	1	1	1	3	3	2
95	2852	3	2	5	7	3	2	1	1	1	1	1	1	1	1	1	1	1	3	3	2

96	2410	1	2	4	1	2	3	1	1	1	1	1	1	1	1	1	1	1	1	3	2
97	2859	2	2	4	2	3	2	2	2	1	1	1	1	1	1	1	1	1	3	3	2
98	2862	3	2	4	4	2	2	2	2	1	1	1	1	1	1	1	1	1	3	3	2
99	2913	2	2	3	6	2	2	2	2	1	1	1	1	1	1	1	1	1	2	3	2
100	2106	1	2	4	1	2	3	2	2	2	1	1	1	1	1	1	2	1	3	3	1

MASTER CHART SCALE

	1	2	3	4	5	6	7
Age (yrs)	< 20	20-30	>30	-	-	-	-
Parity	Primi	Multi			-	-	-
Socioeconomic status	I	II	III	IV	V	-	-
Etiology	Idiopathic	Gestational hypertension	Anaemia	Heart disease	Placenta praevia	Chronic maternal disease	Miscel laneous
Weightgain(kg)	< 5	6-10	> 10	-	-	-	-
AFI (cms)	≤ 5	6-10	11-15	> 15	-	-	-
FL / AC	Normal	Abnormal			-	-	-
HC / AC	Normal	Abnormal			-	-	-
Uterine artery					-	-	-
A) Pattern	Normal	Abnormal			-	-	-
B) High resistance flow	Absent	Unilateral	Bilateral				
C)Early diastolic notch	Absent	Unilateral	Bilateral				
Umbilical Artery							
A) Pattern	Normal	Abnormal					
B) High resistance	Absent	Present					
C) Absent end diastolic flow	Absent	Present					
D) Reversal of flow	Absent	Present					
Middle cerebral artery							
A) Pattern	Normal	Abnormal					
B) Increased diastolic flow	Absent	Present					
Mode of Delivery	Vaginal	Instrumental	LSCS	-	-	-	-
Condition at birth	IUD	Still birth	Live birth		-	-	-
Neonatal complications	Death	Without complication	With complications		-	-	-

Ref. No. 6087 E4 3/2011

Govt.Rajaji Hospital,Madurai.20.
Dated: 10.10.2011

Sub: Establishment-Govt. Rajaji Hospital, aMadurai-20-
Ethics committee-Meeting Agenda-communicated-regarding.

The next Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held at 10.30 Am to 1.30Pm on 26.08.2011 at the Dean's Chamber, Govt. Rajaji Hospital, Madurai. The following members of the committee have attend the meeting.

1.Dr.V. Ramanujam, M.D., D.P.M.,	M.S. i/c Govt.Rajaji Hospital,Madurai.	Convenor
2.Dr.N.Vijayasankaran,M.ch(Uro.)	Sr.Consultant Urologist Madurai Kidney Centre, Sivagangai Road,Madurai	Chairman
3. Dr.P.K. Muthu Kumarasamy, M.D.,	Professor & H.O.D of Medical Oncology(Retired)	Member Secretary
4.Dr.T.Meena,MD	Professor of Physiology, Madurai Medical College	Member
5.Dr.Moses K.Daniel MD(Gen.Medicine)	Professor of Medicine Madurai Medical College	Member
6.Dr.M.Gobinath,MS(Gen.Surgery)	Professor of Surgery Madurai Medical College	Member
7.Dr.S. Thilshadh, MD(O&G)	Professor of OP&Gyn Madurai Medical College	Member
8.Dr.S.Vadivel Murugan., M.D.	Professor of Medicine Madurai Medical College	Member
9.Shri.M.Sridher,B.sc.B.L.	Advocate, 623-B.II.Floor,East II Cross, K.K.Nagar,Madurai.20.	Member
10.Shri.O.B.D.Bharat,B.sc.,	Businessman Plot No.588, K.K.Nagar,Madurai.20.	Member
11.Shri. S.sivakumar,M.A(Social) Mphil	Sociologist, Plot No.51 F.F. K.K. Nagar, Madurai.	Member

Following projects were approved by the committee.

		Obstetrics and Gynecology M.M.C, Madurai.	Tocolysis in preterm labour.	
17	Dr.B.Madeline vihya	PG Student in MD (General Medicine) M.M.C, Madurai.	Study of thyroid dysfunction in systemic lupus erythematosus	Approved
18	Dr.T.Latha Maheswari	PG Student in MD (General Medicine) M.M.C, Madurai.	Study of endometrial thickness by transvaginal sonography with histopathology correlation in abnormal uterine sleeding	Approved
19	Dr.P.K. Muthu kumaraswamy, D.M.	Professor and head of department M.M.C, Madurai.	Study of Docetaxel and Ramucirumab versus Docetaxel and Placebo in the Treatment of Stage IV Non-Small Cell Lung Cancer Following Disease Progression after One Prior Platinum-Based Therapy....Swallowing diary Tamil Translation .	Approved
20	Dr.S. Sreeranjani	II year M.D OG M.M.C. Madurai.	Fetal Doppler Study of uterine, umbilical and Middle are bral artery as predictors of adverse perinatal out come in IUGR as my postgraduate thesis work.	Approved
21	Dr.J.Rekha	Post Graduate in M.D (O&G) M.M.C. Madurai.	Relationship of Placental Pathology to IUGR.	Approved
22	Dr.D. Meena	Post Graduate student in MD (O&G) Dept of Obstetrics and Gynecology M.M.C. Madurai.	Admission Test and it's correlation with perinatal outcome.	Approved
23	Dr.K. Karthikeyan	Post graduate student in General Medicine, VII Medical unit M.M.C, Madurai.	Serum magnesium and end organ damage in type 2 diabetes. from April 2011 To October 2011.	Approved
24	Dr.J. Ramya	PG Student in MD (General Medicine) IV Medical Unit. M.M.C, Madurai.	Diastolic dysfunction in rheumatoid arthritis.	Approved
25.	Dr. B.K. Bincy	PG Student in MD (General Medicine) II Medical Unit, M.M.C, Madurai.	Thyroid dysfunction in rheumatoid arthritis.	Approved
26	Dr. A. Shanmuga sundaram	Post graduate student in General Medicine, V Medical unit. M.M.C, Madurai.	Correlation of electrocardiography changes with prognosis in organophosphorus poisoning.	Approved
27	Dr.T.Gowari Thilagam,	Post-graduate in MD-Pharmacology (II year), M.M.C, Madurai.	Study of the drugs causing fixed eruptios.	Approved
28	Dr.M. Mathivani,	Post-graduate in MD-Pharmacology (II year), M.M.C, Madurai.	Study of Pattern of use and Adverse reactions to Anti snake venom.	Approved
29	Dr.T.Gowri thilagam	Post-graduate in MD-Pharmacology (II year), M.M.C, Madurai.	The effect of Pioglitazone on the distribution of body fat in type II Diabetic Patients.	Approved
30	Dr.S.Shankareswari	Post-graduate in Pharmacology M.M.C. Madurai.	Study on the adverse effects of steroids in patients with nephritic syndrome.	Approved

O.G.

31	Dr.S.RajeshKannan	Post graduate student in General Medicine II Medical unit M.M.C. Madurai.	Rreative protein (CRP) and angiographic correlation of disease in stemi and nstemi patients from April 2011 to October 2011.	Approved
32	G. Angala Eswari	Associate Professor in the PG and Research Department of Economics, Lady Doak College, Madurai.	Maternity Health Care Services at Public and Private Hospitals in Madurai District.	Approved
33	Dr.M. Mathivani	Post-graduate in MD Pharmacology (II year) Institute of Pharmacology, Madurai Medical College. Madurai.	To Study the pharmacoepidemiology of drugs therapeutically prescribed for the patients admitted for cataract surgery in Government Rajaji Hospital, Madurai.	Approved
34	Dr. Mathevan M.D. (Pediatrics)	Principal Investigator Meningitis surveillance Professor of Pediatrics Govt. Rajaji Hospital Madurai	Bacterial Meningitis Hospital based Sentinel Surveillance project.	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution to Government.
2. She/He should inform the institution Ethical Committee in case of any change of study procedure site and investigation or guide.
3. She/He should not deviate for the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events pr Serious adverse reactions.
4. She/he should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and apply for if any Extension of time is required She should apply for permission again and do the work.
6. She/He should submit the summary of the work bto the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the word or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

10/10/11

MEDICAL SUPERINTEND

To

All the above members and Head of the Departments concerned. 10/10/11

All the Applicants.